The development of an English Health-Related Quality of Life (HRQoL) measure for very young children, to be completed by proxy.

By

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VCTJAN001

SUBMITTED TO THE UNIVERSITY OF CAPE TOWN

In fulfilment of the requirements for the degree

PhD in Physiotherapy

Faculty of Health Sciences

UNIVERSITY OF CAPE TOWN

Date of submission:	16 January 2018
Supervisor:	Prof Jennifer Jelsma
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Declaration

I, Janine Verstraete, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise). I declare that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Potential Conflict of Interest:

The Mapping Review of Generic HRQoL measures for children aged 0-7 years and the Systematic Literature Review of Preference based measures for children and adolescents were funded by the EuroQoL Research Foundation (a non-profit organization).
The workshop titled: Exploring the possibilities of developing a HRQoL measure for very young children, held in Cape Town, June 2016 was sponsored by the EuroQoL Research Foundation (a non-profit organization).
The supervisor of this dissertation, Prof Jennifer Jelsma, is a member of the EuroQoL Research Foundation.

Abstract

Background and Aims:

There is an increasing awareness that, in order to monitor health outcomes both mortality and morbidity need to be assessed. A common metric used to measure morbidity and functional limitation is the quality adjusted life year or QALY, which incorporates time spent in a health condition and Health-Related Quality of Life (HRQoL) into the measure. This is of increasing importance in Low Income Countries (LIC) where programmes have been adopted and implemented to address the high burden of child mortality. The 'first 1000 days' is one such initiative which has been adopted by the WHO to improve nutritional support, health care and social support for both the mother and child. One of the aims is to improve quality of life during this vulnerable period. As there is currently no appropriate measure of HRQoL in this age group, we set out to develop a valid and reliable, HRQoL instrument for children from 1 month to 3 years old, amenable to the elicitation of preference weights.

Methods:

The new HRQoL instrument, HRQoL-6D-IT, was based firstly on a mapping review of HRQoL measures for children. The next stage involved eliciting options through cognitive review from caregivers of very young children regarding HRQoL dimensions included in the EQ-5D-Y an existing validated HRQoL measure for older children. The care-givers were requested to identify items to be considered for inclusion, the wording and layout of the new measure. The item pool generated from the literature reviews and cognitive interviews were then assessed through a Delphi study with experts in the field. These items were further reduced through subsequent testing of items and retesting of a preliminary measure. The final items on the HRQoL-6D-IT included: movement, play, pain, relationships, communication and eating and, apart from pain, the descriptors referenced the behaviour of the child to age appropriate behaviour. The HRQoL-6D-IT was then tested for validity and reliability in a group of acutely-ill (AI), chronically-ill (CI) and typically developing (TD) children in two provinces in South Africa: Western and Eastern Cape.

Results:

The methodology used to identify candidate items was rigorous and yielded items which were developed to be observable with dimension descriptors referring to 'age appropriate behaviour'. Caregivers were able to reliably report on HRQoL of their very young children from age 1-36 months.

The content validity had been established during the development of the instrument. Concurrent validity of the different items (dimensions) was tested between the HRQoL-6D-IT and relevant items from the ASQ, FLACC and NIPS pain scale and Diet History. The Kappa co-efficient ranged from 0.33 (fair) to 0.61 (moderate). Known groups were compared (construct validity) and the AI children had the lowest ranked VAS (median 60, range 0-100), indicating worst HRQoL and the TD group was significantly different from AI and CI ($p<0.01$) but AI and CI were not different.
The six items of the HRQoL-6D-IT were tested for internal consistency and reliability and the Cronbach's α=0.83. Test-retest results showed no variance for item scores of movement and play, and high agreement for pain (83%), relationships (87%), communication (83%) and eating (74%). The scores were highly correlated for the VAS (ICC=0.76; $p<0.001$).

Conclusion:
The HRQoL-6D-IT was found to be valid and reliable for use with children aged 1-36 months in South Africa. It is recommended that the HRQoL-6D-IT be included in future research to further investigate HRQoL and the impact of interventions in this vulnerable age group. It is further recommended that future testing be done to assess the feasibility and clinical utility of the measure and to include international input in further development. The lack of stability of the pain dimension needs further investigation. It is hoped that preference based weights will be developed in the future in order to facilitate cost utility analysis of interventions in this vulnerable group.

Keywords: Child, Infant, toddler, pre-schooler, Health, Health-Related Quality of Life, HRQoL, proxy

Acknowledgments

I would like to express my great appreciation to my supervisor, Prof Jennifer Jelsma. She has offered an overwhelming amount of encouragement, guidance and support throughout my research journey. Her passion for research and learning is admirable and has instilled an interest for research in me. I hope to continue my research journey with her support and with the opportunities she has afforded me.

My sincere thank you to my co-supervisor, Prof Lebogang Ramma, for his guidance and support throughout the study.

I would like to extend my appreciation to the EuroQoL Youth Working Group and particularly Michael Herdman and Wolfgang Greiner for their guidance and support throughout the study.

To the wonderful caregivers at all of the research facilities, thank you for your eagerness and willingness to participate in the research. Without your contributions this research study would not have materialised.

Thank you to my colleagues at the Red Cross War Memorial Children's Hospital for supporting and encouraging me throughout this journey. Without your words of encouragement and support I would not have made it through work and my PhD.

To my sister, Mary-Anne Smith, and my mother, Michelle Victor, thank you for your endless assistance with the data collection during the validity and reliability testing of the HRQoL-6D-IT.

To the staff at all of the research facilities, most especially the teachers at the day-care centres, thank you for allowing me to conduct my research at your facilities and facilitating the data collection process.

A special mention needs to be made of my loving husband, Tom Verstraete. His love, support and encouragement carried me throughout this study. He made many sacrifices in the evening and over weekends allowing me to complete this study.

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Abbreviations and Glossary

A/D	Anxiety or Depression
ADHD	Attention Deficit Hyperactive Disorder
ADLs	Activities of Daily Living
AI	Acutely-Ill. Children attending in-patient health care services.
ANOVA	Analysis of Variance
AQoL-6D	Assessment of Quality of Life Six Dimension
ASQ	Ages and Stages Questionnaire (Third Edition)
BASES	Behavioural Affective Somatic Experiences Scale
Beh	Behaviour
CHQ	The Child Health Questionnaire
CHU-9D	Child Health Utility 9 Dimension
CI	Chronically-Ill Children attending out-patient health care services.
Comm	Communication
C-QoL	The Quality of Life Measure for Children
CRIES	Neonatal Postoperative Pain Assessment Score for Crying, Requires oxygen to maintain saturation >95 percent, Increased vital signs, Expression, and Sleeplessness
CUA	Cost Utility Analysis CUA is calculated as the ratio between the cost of a health programme or intervention and the benefit of it in term of the number of years the patient lives in full health. Thus, CUA is when health benefits are expressed as QALYs.
CVI	Content Validity Index
DALYs	Disability-adjusted life years DALYs are similar to QALYs in that they are a numeric representation of life expectancy after adjusting for morbidity. DALY weights however incorporate an age adjustment, based on future economic productivity.
DCE	Discrete Choice Experiment DCE is a technique for eliciting preferences where the responded chooses their preference between a number of hypothetical health states.
DCGM	DISABKIDS Chronic Generic Module
DSQ	DISABKIDS Smiley Questionnaire

ECBQ	Early Childhood Behaviour Questionnaire
Emo	Emotions
EQ-5D	EuroQoL-Five Dimension
EQ-5D-3L	EuroQoL-Five Dimension Three Level
EQ-5D-Y	EuroQoL-Five Dimension- Youth
FDA	Food and Drug Administration The FDA is responsible for upholding and promoting public health and its determinants.
FLACC Scale	Faces, Legs, Activity, Cry, Consolability Observational Pain Scale
HAY?	How are you?
HIV	Human Immunodeficiency Virus
HREC	Human Research Ethics Committee
HRQoL	Health-Related Quality of Life
HSCS-PS	The Health Status Classification for Pre-School Children
HUI	Health Utilities Index
IBQ	Infant Behaviour Questionnaire
ICC	Intraclass correlation coefficient
ICF	International Classification of Functioning, Health and Disability The ICF is a framework for measuring health and disability in both individuals and populations. The ICF was adopted by WHO and its member states in 2001.
ICF-CY	International Classification of Functioning, Health and Disability – Child and Youth
IRT	Item Response Theory
ISOQoL	The International Society for Quality of Life Research
ISPOR	International Society for Pharmacoeconomics and Outcome Research
ITQoL	The Infant Toddler Quality of Life Questionnaire
LIC	Low Income Countries LIC are classified according to their Gross National Income per capita, which amount to $1 025 or less.
LMIC	Lower Middle Income Countries LMIC are classified according to their Gross National Income per capita which is between $1045 and $ 12 736.
LSM	Living Standards Measure The Living Standards Measure is used extensively in marketing research. It was

	developed by the SAARF and is based on a set of marketing differentiators which groups people according to their living standards as opposed to areas based on the size of the community. The measure is based on criteria such as the degree of urbanisation and ownership of assets.
MAP	Multi-Analysis Program
MDGs	Millennium Development Goals
Mob	Mobility
Mvt	Movement
N/A	Not Applicable
NGST	Neuronal Group Selection Theory
NHI	National Health Insurance This is a public health financing system which provides access to health care based on the health needs of the individual irrespective of their financial means.
NICE	National Institute for Health and Care Excellence
NIPS	Neonatal Infant Pain Scale
PCQL	Paediatric Cancer Quality of Life Measure
PD	Pain or Discomfort
PEDI	The Pediatric Evaluation of Disability Instrument
PedsQL	The Pediatric Quality of Life Inventory
PhS	Physical Health Summary score
PIE	Perceived Illness Experience
PIPP	Premature Infant Pain Profile
PROM	Patient Reported Outcome Measure
PROMIS PGH-7	Patient Reported Outcome Measurement Information System Pediatric Global Health
PsS	Psychosocial Summary score
PTO	Person Trade-Off PTO is a technique for eliciting preferences where individuals are asked to choose their preference in treating hypothesised groups of people with health conditions.
QALYs	Quality adjusted life years QALYs assume that one year of life in a health state considered to be perfect is worth one QALY and one year of life lived in a health state which is considered less than perfect is worth less than one.

QoL	Quality of Life
Rel	Relationships
RMSSE	Root-mean-square standardised effect
ROM	Range of Movement
SAARF	South African Audience Research Foundation
SC	Self-Care also categorised by Looking After Myself
SES	Socioeconomic Status
SG	Standard Gamble SG is a technique for eliciting preferences where an individual is asked to choose between remaining in a hypothetical state of ill health for a time period, or choosing an intervention which could either return them to full health or end their life.
TACQoL	The TZO-AZL Children's Quality of Life
TAPQoL	The TZO-AZL Pre-School Children Quality of Life
TB	Tuberculosis
TD	Typically Developing Children attending an open day care centre.
TTO	Time-trade-off TTO is a technique for eliciting preferences where individuals are asked to choose between remaining in a state of ill health for a period of time, or living in perfect health with a shorter life expectancy.
UA	Usual Activities
UCT	University of Cape Town
UK	United Kingdom
UN	United Nations
USA	United States of America
VAS	Visual Analogue Scale
Very young children	Children under the age of three years.
WCHMP	The Warwick Child Health and Morbidity Profile
WeeFim	Functional Independence Measure for Children
WHO	World Health Organisation
WSU	Worried, Sad or Unhappy

1 Chapter 1 – Introduction

1.1 Background

There is an increasing awareness that, in order to monitor health outcomes, both mortality and morbidity need to be assessed. A common metric used to measure morbidity and functional limitation is the Quality Adjusted Life Year or QALY, which incorporates time spent in a health condition and Health-Related Quality of Life (HRQoL) into the measure [1]. The World Health Organization Quality of Life Assessment (WHOQOL) group defines Quality of Life (QoL) as "an individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [2] page 1403. Health-Related Quality of Life (HRQoL) can be considered a component of QoL, which can be measured by the impact the subjective perception of physical, emotional, mental and social functioning has on QoL [3], [4]. There are many measures of HRQoL which have been developed for older children and adults, but there are few validated measures for infants and young children. This thesis documents the process and validation of such a measure.

1.1.1 Extent and Nature of the Problem

In Africa, children under five years of age comprise 16,5% of the total population [5]. They also bear the highest burden of disease, with a mortality rate of 51% [5] attributed to primarily poor nutrition, diarrheal disease, pneumonia, Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) [5]. The World Health Organisation (WHO) adopted the United Nations (UN) Millennium Development Goals (MDGs) in an effort to in part combat this issue[6]. The MDGs consisted of eight goals that the UN member states agreed to achieve by the year 2015. These goals committed member states to combat poverty, hunger and disease amongst others [6]. To date these goals have been partially met globally, but child mortality and maternal health are still two key issues faced by many Low Income Countries (LIC) and Low Middle Income Countries (LMIC) [6]. New Sustainable Development Goals (SDGs) have been launched by the WHO with a target date of 2030 [7]. The third SDG aims to ensure healthy lives and promote well-being for all at all ages and includes areas or reproductive, maternal, new-born and child health [7]. In response to this the "First 1000 Days" initiative aims at further reducing the burden of maternal health and child mortality [8], [9]. The "First 1000 days" of life is characterised from conception to two years of life. This is a vulnerable but instrumental period for optimal growth, brain development and health. This period lays the foundation for the child's life, however; this foundation is often weakened in LIC and LMIC by the determinants of poverty,

environmental and societal hardships, ill-health and malnutrition [10], [11]. The programme is focused on nutritional support for both mother and child, access to quality health care, clean water and sanitation and social support systems. One of the aims of the initiative is stated as "improvement of care and quality of life during the first 1000 days" [9] page 1. This programme has been adopted by the WHO and was launched by the South African Departments of Health and Social Development in February 2016 [8]. The need to promote this in South Africa is of paramount importance as the country did not meet their MDG for decreasing child mortality and improved maternal health [9]. Measurement of mortality is less complex and routine in most countries; however the effects of morbidity are not often recorded. Morbidity results in considerable burden on health and social resources as well as a high burden of care for the family and society. HRQoL measures can assist in evaluating and monitoring the burden associated with morbidity and can therefore be useful measures to assess progress made in addressing the relevant MDG.

1.1.2 Health-Related Quality of Life in Very Young Children

HRQoL measures aim to capture the subjective multi-dimensional constructs of QoL namely physical, social and psychological functioning which are relevant to health [2], [12]. The dimensions included in a HRQoL measure are generally developed in consultation with the intended target group of the instrument [12]–[15]. There has been an increase in the development and use of HRQoL measures as they are considered valuable in improving patient health and in valuing healthcare [15], [16].

The use of HRQoL measures is broad and includes: population health surveys, burden of disease studies, epidemiological studies, screening, describing health status, developing management plans for individual patients, informing clinical policy and resource allocation decisions [16]–[22]. The use of HRQoL measures can further be used to evaluate HRQoL between individuals at a single point in time and within a patient over time [14]. These are important characteristics to consider especially if the HRQoL measure is being used within a clinical trial [14], [15].

There are two categories of HRQoL measures: generic and disease-specific measures. Generic measures can be used in a wide variety of health conditions and the dimensions thus need to apply to diverse conditions and populations [12], [14]–[16]. Thus, generic measures are able to compare HRQoL across different health conditions or populations. Generic measures can be used as either health profiles or preference-based measures. Health profiles generally score each dimension separately. They form the basis for the development of preference-based measures which obtain a single summary index or utility score which reflects the preferences for different health states as described by the HRQoL measure [23]. Preference based measures are health profiles which are particularly useful for economic evaluation as they have a

preference based score. For example, the United Kingdom's (UK) National Institute for Health and Care Excellence (NICE) uses a preference based generic measure to guide the National Health Insurance (NHI) in assessing new drugs and treatments [24]–[26]. NICE is guided by economic evaluation which typically includes Cost Utility Analysis (CUA) where health benefits are expressed as QALYs, based on the EQ-5D, the HRQoL measure developed by the EuroQoL Research Foundation (see below) [24]–[26].

In contrast to generic HRQoL measures, disease-specific measures have dimensions which are specific to the symptoms of the health conditions being measured and may provide greater sensitivity and specificity to the HRQoL of the individual with the health condition in question [12], [14]–[16].

Due to the subjective nature of HRQoL it is encouraged, that as far as possible, individuals report on their own HRQoL [13], [27]. As the sequelae of a health condition are specific to each individual and are known only to them, evaluation of their perspective is key to capturing their experience of the health condition and the management thereof [13]. An instrument which evaluates HRQoL from the patient without interpretation of their response by a second party is categorised as a patient-reported outcome measure (PROM). It is widely recognised that there are a group of individuals who are too young or cognitively unable to complete PROMs and thus in some cases it is necessary to rely on measurement of HRQoL instruments through proxy report [13], [16], [27]–[32].

The use of measurement of HRQoL in children and adolescents has increased in the last two decades [14]. Connolly and Johnson (1999), have highlighted that the main difference between HRQoL measures developed for adults and children lies within the development of the dimensions [14]. The activities and experiences of children differ substantially from that of adults as well as between different age groups of children [14]. Thus, one needs to consider the dimension of HRQoL of children according to the activities which are developmentally appropriate for the age group of children in question [14]. This does pose challenges as children are continually changing and developing [14]. In addition, poor health in children may not necessarily be measured by absence or abnormal functioning but rather by a delayed achievement of developmental milestones [14].

The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) task force has developed guidelines for good research practice for the development of HRQoL measures [13]. They have recommended that the HRQoL of children less than five years of age should be measured by observational reports from parents or other adults [13]. Observational reports can be characterized as a measure, completed by an adult, based on the observed behaviour of the child as opposed to the subjective rating of the adult on the child's capabilities [13]. This is in accordance with the Food and Drug Administration (FDA)

guidelines for PROM development [33]. ISPOR further recommends that dimension development for the very young age group (less than five years of age) should be based on focus group or cognitive interview results with parents of these children to ensure content validity [13]. Proxy measures have been developed for completion by caregivers to assess the HRQoL of children, who are too young to self-report [27], [34]. Although differences in self-report and caregiver proxy report have been found in older children both viewpoints are considered important [27], [35]. Furthermore, the caregiver's perspective is important as they are often making health care decisions for the child [13]

With the intention of developing a valid and reliable HRQoL measure in young children and infants, the researcher thus set out to explore the following questions. Are there published HRQoL measures available for very young children? And if so, are they psychometrically sound? What dimensions and specific items are included and how were they identified? If, as was anticipated, there are no appropriate measures for this age group, what items should be included and what process should be used to identify these items? Would it be possible to develop a "one size fits all" measure for children under three years of age or would it be necessary to have different dimensions and items for different age groups? Once appropriate items were identified and a new HRQoL measure developed for infants and younger children, would it be relevant, valid and reliable across all age groups?

1.2 Aims and Objectives of the Thesis

There were three overall aims for the thesis, which are listed below with their corresponding objectives.

1. The first aim was to investigate the need for a psychometrically sound HRQoL measure for very young children. The specific objectives were:
    - To establish what measures were available for use in children younger than seven years of age.
    - To establish if there was a specific age group for which a new measure was required. This was investigated by reviewing the literature.
2. Secondly the study aimed to develop a new English HRQoL measure for very young children. The objectives related to this aim included:
    - To identify a suitable bank of items. This was established through a number of steps including: literature review, cognitive interviews with caregivers and expert opinion.
    - To identify age-appropriate descriptors for each domain to ensure observability. This was established through review of the literature, cognitive interviews with caregivers and expert opinions.

- To prune the item bank to the smallest number of important domains for validity and reliability testing. This was achieved through expert opinion, review of the literature and conceptual framework, expert opinion and testing of items.

3. The final aim was to determine if the psychometric properties of the new English HRQoL were acceptable. The specific objective related to this aim was:
   - To establish the concurrent validity, discriminant validity, feasibility, acceptability and reliability of the new instrument.

1.3 Significance and Justification of the Study

The burden of disease in South Africa, as in most LMIC, is highest in the youngest age group of children between 0-5 years [5], [11], [36], [37]. It is hoped that this thesis will result in an appropriate outcome measure for this age group that has been validated in a LMIC. Cape Town is home to the only dedicated tertiary paediatric hospital in Sub-Saharan Africa with referrals from across South Africa and the borders of Africa (see below under Research Setting). The majority of the patients who visit the hospital are from the poor and marginalised communities, which is an important consideration as this is where the efforts to reduce childhood morbidity and mortality are focussed [8] .

In the South African context, a generic HRQoL would have benefits in informing health status across the population, measuring the progress of health technology and services across the country or within an institution or service, informing policy development and health economic evaluations. As the measure is intended to be compact and generic, it can also be utilised in the clinical setting to monitor the impact of interventions on individual patients either in clinical trials or in routine clinical data collection.

The development of a psychometrically sound HRQoL measure would allow for the development of preference weights for different health states as described by the measure and thus for the calculation of QALYs to be used in monitoring the burden of disability due to different conditions. Once preference weights have been developed[1] the measure would allow for comparison of the relative cost-effectiveness (CE) of different technologies in order to inform resource allocation. Currently South Africa does not routinely use any HRQoL measures in clinical practice nor are preference based measures used for health economic evaluations [38]. The development of a short, clinically relevant and accepted outcome measure may be viewed favourably for use as a routine outcome measure in South Africa.

[1] There is on-going collaboration with the EuroQoL Foundation and it is possible that the Foundation will develop preference based values in the future.

The health care system in South Africa is however being reviewed and there is a proposal for NHI for the near future [38]. Thus, the use of preference based measures may be one of the options for the government to consider for informing choices regarding the allocation of health resources.

In conclusion, an instrument to monitor HRQoL and thus effectiveness of health interventions in very young children has the potential to allow clinicians, researchers and policy makers to make better decisions with regard to the management of children. It would serve as the first step towards developing a preference based measure as validated, reliable items would be available to describe the different health states that could be valued. It would be of use both locally and internationally.

1.4 Research Setting and Context

The impetus for this thesis arose out of the involvement of the researcher and her supervisors with the EuroQoL Research Foundation which is a non-profit organisation responsible for research into economic assessment of health interventions based on measurement of HRQoL. The Foundation has developed a stable of generic measures to measure HRQoL in adults and older children, including self-report and proxy versions. Although developed in Europe initially, the measures are now used internationally, with the different versions available in over 150 languages [39]. The EQ-5D (adult version) and EQ-5D-Y (youth version) have both been validated in South Africa and are available in six of the eleven official languages [39]. The EQ-5D and EQ-5D-Y have been utilised in LMIC making comparison easily accessible[39].

The adult version, the EQ-5D is a preference based measure which is used extensively in CUA, such as that done by NICE to inform resource allocations [39]. In addition, it is employed as an outcome measure in many different clinical trials, sponsored by pharmaceutical companies. A project is underway to develop preference weights for the EQ-5D-Y version [39]. Although the EQ-5D-Y, a youth version has been developed, with an extended proxy version to children aged four years and older, the proxy version has been poorly researched with only two Spanish studies on the validity of the measure [40]. Following an extensive literature review, the EQ-5D-Y Proxy was used to start the conversation with care-givers regarding an appropriate item bank for the younger children. The Foundation has sponsored portions of this research, including the mapping review and a two-day workshop in Cape Town in June of 2016, attended by both local and international experts in the field of HRQoL in children to explore the feasibility of such an instrument. The deliberations of this workshop further informed the choices made with regard to item bank, descriptor levels and target respondents.

Much of the research took place at a children's hospital in Cape Town which was the only dedicated tertiary paediatric hospital in Sub-Saharan Africa. The hospital has over 260 000 patient visits per year with referrals from the Western Cape, South Africa and across the borders of Africa. The majority of the patients who visit the hospital are from the poor and marginalised community. The literacy level in this community is generally lower due to the historical differences brought about by apartheid. Thus, a measure developed in this community would be simple and comprehensible and thus accessible to caregivers of all levels of literacy.

As the format of the questionnaire is similar to the EQ-5D-Y format with regard to layout and font, permission was granted by the EuroQoL Research Foundation to use this format in the presentation of the draft questionnaire.

1.5 Outline of the Thesis

The first chapters consist of a narrative and a mapping review of the literature. The narrative literature review (Chapter 2) explores the basic concepts relevant to HRQoL including differences between HRQoL, health status and functional measures; the difference between generic and preference based measures, the problems associated with proxy report and identifying a suitable conceptual framework for a new measure.

Before identifying items and a structure for a new measure it was necessary to investigate the literature to determine whether there was a need for a new measure and how the other measures were developed. To this end, a mapping review of generic HRQoL measures for children was undertaken (Chapter 3)[2].

Chapter 4 describes the process of item identification. Based on the narrative and mapping reviews, coupled with the experience of the researchers with the instrument, the EQ-5D-Y was identified as an appropriate starting point. The proxy version of the measure was newly developed and there was little published on the validity or reliability thereof. Thus, the measure was tested in cognitive interviews of caregivers of children under the age of seven years. As the EQ-5D-Y is used in children as young as seven years for self-report, it was important to investigate the performance of the proxy version in younger children before proceeding with the development of a further measure. The layout, structure and wording of the EQ-5D-Y were also investigated. The results of the cognitive interviews showed that the existing

[2] Note that this review was done as part of the student's registration for an MSc in Physiotherapy. As it was found that there were no suitable measures, the student upgraded to a PhD to develop the new measure.

dimensions were appropriate for children aged over three years of age. Thus, the decision was made that the greatest need was to develop a new measure for children aged from birth to three years.

The candidate items were identified through both the mapping review of generic and preference based measures and cognitive interviews with caregivers of children. The number of items was reduced through a two round Delphi study with experts in the field. The experts also suggested labels for the dimensions and dimension descriptors for the questionnaire (Chapter 5).

Chapter 6 discusses the development of the Alpha Draft from the identified items and the subsequent testing to further reduce the items. The results revealed that the items needed to be further reduced to six items; however the wording of some of the items also needed to be changed to better represent all of the age groups of children from 0-3 years. Thus, the Beta Draft was developed and the structure of the questionnaire was investigated.

The final Delta Draft was then tested for validity, reliability and feasibility (Chapter 7). The discussion of the process of instrument development as outlined in the preceding chapters is presented in Chapter 8, together with the conclusions arising from the study and recommendations for future practice and research.

2 Chapter 2: Narrative Literature Review

2.1 Introduction

HRQoL is a contested concept and there are many different opinions as to what is encompassed. In order to understand HRQoL, it is necessary to first explore the meanings of health and disease and to define QoL in general and then to contextualise HRQoL within an appropriate framework. As the focus of this thesis is young children, an understanding of the different developmental theories is also necessary to ensure that the unique aspects of the developing infant can be captured by a HRQoL instrument.

The development of an appropriate measure for measuring HRQoL in very young children should take place taking cognisance of the different theoretical approaches but it should follow a rigours methodology. Authors have summarised the steps necessary for the development of valid instruments [41]–[43] and the use of tested methodology employed in each of these steps is necessary to ensure a psychometrically sound measure [44].

The aim of the narrative literature review was thus to draw on published papers to identify a working framework which would inform the development of a new measure. The specific objectives were:

- To explore the concepts of health, health status, QoL, well-being, HRQoL and functioning, with particular regard to the application of these concepts to younger children.
- To investigate the different approaches to measuring health, health status, well-being, QoL and HRQoL and functioning in order to select a basis for measurement for the new instrument.
- To explore the nature of HRQoL measures including differences between generic and disease specific measures, choice of respondent (self/proxy), and the role of preference based HRQoL measures.
- To review relevant conceptual models as a basis for selecting a theoretical conceptual framework on which to develop the new measure.
- To review relevant models and theories of universally accepted child development to inform the theoretical basis of item generation and descriptor development for the new measure.
- To identify an appropriate methodology for developing an item pool, possible scoring systems and validation of the instrument.
- Finally, to review the role of HRQoL measures globally and in South Africa.

2.2 Methodology

The methodology used for this review was that of a narrative literature review, which according to Grant and Booth (2009), describes "published materials which provide an examination of recent or current literature. Review articles can cover a wide range of subject matter at various levels of completeness and comprehensiveness based on analyses of literature that may include research findings. Generally, a literature review involves some process for identifying materials for potential inclusion—whether or not requiring a formal literature search—for selecting included materials, for synthesizing them in textual, tabular or graphical form and for making some analysis of their contribution or value" [41] page 97.

It has been noted that this methodology might limit the reproducibility of the study and that additional bias such as selection and evaluation bias may be introduced [45]. However the use of a well-defined search strategy may have minimised the impact of these limitations on the study.

2.2.1 Search Strategy

The following electronic databases were searched: Academic Search Premier, Africa-Wide, CINAHL, ERIC, Health Source- Nursing/academic edition, NiPAD, The Cochrane Library, PEDro, PsychArticles, PsycInfo, PubMed (which includes Medline), Scopus (which indexes Embase), Web of Science and Science Direct. The only limit to the searches was the inclusion of English articles or abstracts. No limits were set regarding dates of articles as important information could have been missed if excluded. Suitable academic books were used. Pearling, which entails using the literature at hand to identify additional relevant studies, was done by hand searching the references of sourced papers. The websites of identified measures were also consulted for additional manuals or reference papers. Search terms used to identify articles related to the objectives included:

- To explore the concepts and different approaches to measuring: health, health status, well-being, QoL, HRQoL and functioning in order to select a basis for measurement for the new instrument. ("Health" OR "Health-Related Quality of Life" OR "Quality of Life" OR "well-being" OR "health status" OR 'function*) AND ("children" OR "paediatric" OR "pediatric" OR "infant*" OR "child*") AND ("questionnaire" OR "instrument" OR "measur*"). ("Health-Related Quality of Life", OR "Quality of Life" OR "well-being" OR health status") AND ("valuation" OR "QALYs" OR "Cost Utility Analysis" OR "Cost Effictiv*") AND ("generic" OR "preference-based") OR ("validation" OR "develop*").

- To explore the nature of HRQoL measures including differences between generic and disease specific measures, choices of respondents (self/proxy, and the role of preference based HRQoL measures. ("Health-Related Quality of Life" OR "Quality of Life" OR "well-being" OR "health status") AND ("children" OR "paediatric" OR "pediatric" OR "infant*" OR "child*") AND ("questionnaire" OR "instrument" OR "measur*") AND ("generic" OR "preference-based" OR "disease") OR ("proxy" OR "observable") OR ("valuation" OR "QALYs" OR "Cost Utility Analysis" OR "Cost Effictiv*")
- To review relevant models and theories of universally accepted child development. ("Child", OR "Paediatric" OR "Pediatric") AND ("development" OR "theories" OR "milestones" OR "Gross Motor" OR "Fine Motor" OR "Cognitive" OR "Attachment" OR "Psychology")
- Discuss and select a theoretical conceptual framework on which to develop the new measure. ("Health-Related Quality of Life", OR "Quality of Life" OR "well-being" OR "health status") AND ("psychometric" OR "properties"). ("Health-Related Quality of Life", OR "Quality of Life" OR "well-being" OR "health status") AND ("Definition" OR "Conceptual Frame*")
- To identify an appropriate methodology for developing an item pool, possible scoring systems and validation of the instrument. ("Health-Related Quality of Life" OR "Quality of Life" OR "well-being" OR health status") AND ("children" OR "paediatric" OR "pediatric" OR "infant*" OR "child*") AND ("questionnaire" OR "instrument" OR "measur*") AND "generic" OR "preference-based" OR ("validation" OR "develop*")
- To review the role of HRQoL measures globally and in South Africa. ("Health-Related Quality of Life", OR "Quality of Life" OR "well-being" OR health status") AND ("Africa" or "South Africa"). ("Health-Related Quality of Life", OR "Quality of Life" OR "well-being" OR health status") AND ("import*")

The articles were read by the researcher and the contents synthesised and analysed to address the aims of the review.

2.3 Results and discussion

2.3.1 Introduction

There is a complex relationship between health, functioning in daily life and well-being [42], [43] and in order to understand the concept of HRQoL all of these concepts need to be interrogated. The definition of health is not trivial as in many cases the definition of health determines the outcome measures used to determine the success of intervention [44] and the consequences of subscribing to one or other conceptualisation on the nature of health care provided are considerable [45]. The first part of this review

deals with the conceptual understanding of the important constructs related to health. The construct of health is first discussed and the related constructs of well-being and QoL. As HRQoL is the focus of this thesis, this is discussed in detail and the different models used to unpack this concept and the different attributes of HRQoL measures are described. Functioning is also related to health and this is explored in relation to HRQoL. As the mooted instrument was to be used in very young children, the theories of child development are also briefly discussed with the concomitant implications for developing a HRQoL measure in this group of subjects.

This is then followed by an exploration of the process by which new self-reported outcome measures should be developed in order to guide the development of the proposed new instrument for younger children.

2.3.2 Review of Concepts: Health, Health Status, Well-being, QoL, HRQoL, Functioning and Child Development

2.3.2.1 Conceptualisation of Health and Health State

In 1948 the WHO, in its constitution, defined health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" [46] page 1. This was an important milestone as it marked the beginning of a global movement away from the biomedical model of health which emphasised the role of disease or symptoms in determining health [19], [47], [48]. The biopsychosocial model of health which recognises that psychological and social factors are important determinants of health began to get more recognition [45], [48].

Although ground breaking at the time, the WHO definition has been criticised as setting an unattainable goal for any healthcare system and as an unintended consequence, leading to the over medicalisation of society as more and more risk factors for different disease conditions are identified and regulated [49]. This definition is also not appropriate as it "minimises the role of the human capacity to cope autonomously with life's ever changing physical, emotional, and social challenges and to function with fulfilment and a feeling of well-being with a chronic disease or disability" [42] page 236. In the Ottawa Charter of 1986, the WHO redefined health as: "Health is … seen as a resource for everyday life, not the objective of living. Health is a positive concept emphasizing social and personal resources, as well as physical capacities. Therefore, health promotion is not just the responsibility of the health sector, but goes beyond healthy life-styles to well-being" [50] page 1 .

Sartorius (2006), recognised three possible definitions of health: the absence of any disease or impairment; "a state that allows the individual to adequately cope with all demands of daily life (implying also the

absence of disease and impairment) and a state of balance, an equilibrium that an individual has established within himself and between himself and his social and physical environment" [45] Page 662. The third definition would thus address the need for a definition of health that addresses the health state of those with chronic health conditions, who, despite having an underlying health condition, such as diabetes mellitus or hypertension may still regard themselves as healthy. The recommendations arising out of a meeting of experts convened by the Health Council of the Netherlands in 2010 to discuss the construct of health, reiterated this [42]. It was recommended that health should be conceptualised as "dynamic, based on the resilience or capacity to cope and maintain and restore one's integrity, equilibrium, and sense of wellbeing" [42] page 343.

With the increase in chronic diseases and the ageing of the population, the health of many, in medical terms, may eventually prove lacking and the ability to attain maximum possible functioning in daily life and well-being will become increasingly important [42]. These concepts need to be further discussed. As the conceptualisation of health changed, so too have the measures used to monitor the impact of interventions and describe the health of populations. These indicators may be objective or subjective and these two areas do not necessarily overlap. "Age-related impaired functioning does not strongly influence self-rated quality of life" [44] page 10. The measurement of disease within a medical model includes mortality rates and objective measures such as markers of disease, e.g. systolic and diastolic blood pressure in hypertension or the blood glucose in diabetes mellitus. This biomedical approach to disease measurement has however been criticized as it only accounts for the signs and symptoms of a disease which was thought to arise from a physical abnormality in the body or its functioning [48] and does not address the concerns raised above with regards to chronic diseases. It has thus been recommended that measures of disease markers or symptoms no longer be taken in isolation and should be combined with other holistic measures to determine the impact the disease has on the patient [19], [28], [47], [51], in other words subjective measures of health are increasingly recognised as of being importance.

Many health measurement strategies have been employed to be used alongside medical markers of health [52]–[55]. The objective measure of health status is one measurement strategy to assess the impact which health has on physical functioning [23], [28], [47], [56], [57]. Patrick and Bergne (1990), described the measurement of health status as the distinction between so-called normal conditions, which were widespread, and pathological deviations,which were classified as conditions that deviated from the norm [58]. Thus health status measures would evaluate any "undesirable deviations from the expected activities or perceptions that constitute usual daily life" [58] page 166. This definition was much debated as health-care managers and policy-makers became more interested in the measurement of health and health status [59]. Thus the definition was expanded to include distinction between physical and mental dimensions of

health, and health was defined as ranging and not merely the deviation from the norm [59]. As a result of this definition health status measures often have dimensions which include aspects of physical, psychological and social functioning which are likely to be affected by the health state [23], [28], [47], [56], [57]. Health status has been regarded, by some, as a measurement that can be confirmed by a third party, such as a clinician or caregiver [60]. An example of a health status measure for Juvenile Rheumatoid Arthritis (a systemic condition which frequently results in joint damage) would include the disease specific change in gait or Range of Movement (ROM) in an affected joint [61]. Typically only the ability and quality of gait will be assessed by a health status measure rather than the ability to get from point A to point B by another means such as in a wheelchair [28], [47], [57]. Measurement of health status does not however take into account the individual's perception and reaction to their health status and other nonmedical aspects of their lives as would be measured by QoL [43], [62].

2.3.2.2 Well-being and Quality of life

Including measurement of psychosocial issues, as captured by QoL and well-being, in addition to health indicators is an important predictive factor in patient outcome and is further important to measure when evaluating treatment [63]. QoL and well-being are often used interchangeably which could be attributed to the fact that they both consist of objective and subjective components [63]. It was proposed that well-being refer to the "objective life conditions that apply to a population generally, while quality of life should more properly be limited to individuals' subjective assessments of their lives" [63] page 151.

The Oxford English Dictionary further suggests that well-being concerns a community or population in its definition "with reference to a person or community: the state of being healthy, happy, or prosperous; physical, psychological, or moral welfare" [64].

Social well-being is one of the better described terms in the literature and is said to encompass three main concepts: "evaluation (life satisfaction), experience (momentary mood) and eudemonia (purpose)" [65] page 409. These aspects of social well-being are further explained by Stiglitz et al (2009) as "cognitive evaluations of one's life, positive emotions (joy, pride), and negative ones (pain, worry, anger). While these different aspects of subjective well-being have different determinants, in all cases these determinants go well beyond people's income and material conditions" [66] page 216. There is growing interest (in the UK) in incorporating social well-being into economic and social policy [66]. There are three broad categories of measurement that policy makers have adopted to measure social well-being which is similar to the definition above and includes: evaluation, experience and eudemonic. Life satisfaction (evaluation) is the most researched and has been shown to be correlated with income (both absolute

and relative), employment status, marital status, health, personal characteristics (age, gender, and personality) and major life events" [66] page 414. Experience or momentary mood is more challenging to measuring as it is viewed as "the average balance of pleasure (or enjoyment) over pain, measured over the relevant period" [66] page 415. Challenges include evidence which suggests that positive and negative emotions are independent and need to be measured separately. Furthermore the measurement is confounded by 'mind wanderings' where one's thoughts wander between current activities and other worries about unrelated things [66]. The measure of eudemonia or purpose is based on Eudemonic theories with suggest that individuals have "underlying psychological needs, such as meaning, autonomy, control and connectedness contribute towards wellbeing independently of any pleasure they may bring" [66] page 417. Measurement of purpose is made on how subjectively much meaning one's life has in response to certain constructs [66].

Social well-being is often measured in terms of happiness of the individual [67], [68]. Happiness is included in the Oxford English Dictionary [64] definition of well-being (as above) as well Mayo's dictionary definition of QoL which "according to Aristotle, quality of life would be the best kind of life, the happiest life..." [62].

QoL is however not only used interchangeably with well-being as Mayo's dictionary (2015) further alludes to the erroneous interchange of the terms of QoL, HRQoL or health status and states that QoL is " broader than just health and includes components of material comforts, health and personal safety, relationships, learning, creative expression, opportunity to help and encourage others, participation in public affairs, socializing, and leisure" [62]. Ware (1995) discusses that the erroneous labelling of all measures of health into a single category of QoL as a shorthand method used by many to refer to any concept which was broader and more qualitative than biological measures of health [59]. Ware (1995) further discusses that QoL is a more extensive concept than health as it "encompasses standard of living, quality of housing and neighbourhood, job satisfaction, health, and other factors" [59] Page 328.

The range of QoL definitions is extensive and could be attributed to wide range of components which individuals find important [69]. QoL is defined by the WHO as a "broad ranging concept, incorporating in a complex way individual's physical health, psychological state, level of independence, social, relationships, personal beliefs and their relationship to salient features of their environment" [2] page 1405. Felce & Perry (1995) described a model of QoL based on five dimensions namely: physical wellbeing, material wellbeing, social wellbeing, emotional wellbeing and development and activity [69]. This model integrated both objective and subjective dimensions and states that "externally derived norms should not be applied without reference to individual differences" [69] page 51. However the measurement of QoL would allow for "objective comparisons to be made between the situations of particular groups and what is normative"

[69] page 51. HRQoL can be distinguished from QoL as it is focussed on the factors which encompass the health care systems [60].

2.3.2.3 Health Related Quality of Life

HRQoL is often termed as a multidimensional measurement approach [47]. This multidimensionality is subsequent to the WHOs definition of health which includes three dimensions of health: physical, mental and social [71]. The three dimensions of health and an additional dimension of functional status have been combined to form the four, generally accepted, dimensions of HRQoL: disease and symptoms thereof, health status, psychological and social functioning [47]. These dimensions are universal across the lifespan.
Most definitions of HRQoL place importance on the perceived effects of health on physical, social/role, psychological/emotional, and cognitive functioning. Disease symptoms, perceptions of health, and overall QoL are often included within the dimensions of a HRQoL measure [34]. HRQoL can be regarded as the perceived effect which a medical condition or its management has on a person which can be either general or specific to the health condition. HRQoL, rather than the more general QoL, forms the target of this thesis.

In light of the discussion above it is important to develop a definition of HRQoL in the target group which will inform the conceptual framework. The measurement of HRQoL in cancer has been a focus in the development of many HRQoL measures [18], [72]–[74]. Many of these cancer specific measures have subsequently been validated as generic HRQoL measures [73], [75], [76]. However, one of the obstacles identified in developing a new generic measure of HRQoL for children is the fact that children function from a different developmental viewpoint than adults and thus need a unique conceptual framework [77]. Many of the definitions of HRQoL for adults and generic profiles were not accepted thus a modification was suggested "(HR)QoL includes, but is not limited to the social, physical and emotional functioning of the child and adolescent, and when indicated, his/her family, and it must be sensitive to the changes that occur throughout development" [78] page 1334. This definition will inform the conceptual framework for the new measure.

There are a number of accepted HRQoL measures for children aged seven years and older. There are very few measures developed for the very young child and where developed they have not included a conceptual framework or a different definition of HRQoL for this age group [18], [34], [60]. This is explored in a separate literature review (see Chapter 3).
A conceptual framework for the development of a HRQoL measure should guide the development of a new measure. It is suggested that the conceptual framework should include: the definition of HRQoL to be used

in the measure, theoretical framework in which item development should be considered, process of item generation, generation of dimensions from items, wording of dimensions, preferred number of items format for response options, the time frame in which to consider the dimensions, scoring system for the measure and psychometric properties to consider [15], [16], [23], [47], [79]–[84]. Considering the target group of very young children these would need to take into account the rapid development during this period of life as well as their attachment to the primary caregiver for health and health decisions [60], [85]. Many of these issues were discussed with experts in the field of paediatrics and HRQoL during the two day workshop sponsored by the EuroQoL Research Foundation [86]

2.3.2.3.1 The Role of Health-Related Quality of Life Measurement

Measurement of HRQoL in very young children is becoming more and more important. Mortality in the under five years age group is high globally, but markedly so in LIC and LMIC [5], [87]. Child and Infant mortality rate is a universal indicator of health status of a population and this age group suffers the highest burden of disease [87]. According to the Global Burden of Disease Study in 2001 deaths of children under five years of age accounted for nearly 20% of the overall mortality rate [5], [37]. 99% of the deaths recorded in children under five years were recorded in LIC and LMIC; more than 40% of those deaths occurred in Sub-Saharan Africa [37]. The greatest cause of mortality in this age group in LIC and LMIC is attributed to poor nutrition, diarrheal disease, pneumonia, malaria, TB and HIV [5], [36], [37], [87] As discussed in the Introduction, the 'First 1 000 Days' initiative has been adopted by the WHO and its member states to address the MDG [8], [88]. This initiative was recently launched in South Africa and aims to reduce child mortality and improve maternal health through nutritional support for both mother and child, access to quality health care, clean water and sanitation and social support systems [9]. Whereas measures of HRQOL should not replace the traditional measures of morbidity (prevalence of chronic disease or disability usually recorded in country or regional registries), they should complement these and become part of the standard battery of tools used to assess the health and well-being of adults and children [16], [19], [20], [60].

A preference-based measure could further assist in evaluating the cost and impact of large scale interventions that are likely to be implemented in response to the WHO [16], [19]–[22]. Technologies which decrease mortality and morbidity are now more widely available, albeit at a large cost (e.g. neonatal intensive care support, management of terminal diseases). Decisions regarding care need to be made at both a health authority and individual patient level [15], [19], [20]. With the improved technologies for care one also needs to determine not only the reduced morbidity but the associated sequelae of improved treatments or survival from diseases such as pneumonia, TB and HIV [20], [21]. This could further assist in

the design of new therapies or technology in balancing the reduction in morbidity without compromising survival rates. It is suggested that these morbidities can be measured with HRQoL measures [18].

HRQoL measures could further serve as a useful tool in developing management plans for individual patients in the clinical setting [16]. As HRQoL measurement during the course of treatment could provide important information to families and clinicians when assessing the effectiveness of the treatment and the subsequent effect on the child's HRQoL [16], [18]. This could also become important when the side effects of the preferred treatment are impacting negatively on the child's HRQoL and one needs to consider an alternative treatment. The goal of any treatment should be to make the child feel better and thus enhance the child's HRQoL [18]. Thus, HRQoL measures can complement clinical and physiological measures as often the treatment may be effective without the child feeling better [18], [19]. If the HRQoL measure is completed before consultation with the clinician it could also offer important guidance to the clinician on where to focus their attention during the limited time of the consultation [16], [18]. This could be achieved with either a generic or preference based HRQoL measure. However, one needs an age-appropriate and sensitive HRQoL in order to achieve these goals [13], [16], [18]. In the paediatric population this often needs to be done with proxy measurement.

2.3.2.3.2 Models of HRQoL

Wilson and Cleary Model

HRQoL measures have been used in clinical trials and in effectiveness research on the premise that pharmacological therapies can affect parameters of HRQoL [12], [16], [47]. HRQoL measures were used for this purpose but before Wilson and Cleary (1995) set out to explore the relationship between clinical variables and HRQoL there was no known relationship [89]. At the time this model was created there were two models of health: the biomedical model and the QoL model [89], [90]. The biomedical model focussed on the cause of illness from a physiological level in order to effectively treat it. In contrast, the QoL model focussed on the dimensions of functioning and there was a drive to understand the complex behaviours and feelings which were associated with ill health [89]. Wilson and Cleary (1995), set out to combine these two models of health into a valid description of health and represent the relationship or causal pathway between different health concepts [89].

The Wilson and Cleary model (Figure 2-1) comprises of five constructs: biological and physiological factors, symptoms, functioning, general health perceptions and overall QoL [89]. Although there are arrows in the figure, they do not imply that there are no relationships between the different levels and characteristics of the individual or environment [89]. The level of biological and physiological factors would include the

health condition as well as objective or clinical measures of the disease such as blood pressure or a blood glucose level. Symptoms are defined as "a patient's perception of an abnormal physical, emotional or cognitive state" [89] page 61 and would include any perceived effect on these dimensions from the health condition. Functioning would be assessed by the individual's perceived capacity of fulfilling Activities of Daily Living (ADLs) such as self-care, mobility or broader functions within the community. General health perception would include the perceived effect of their health on the criteria above and on the individual's mental state. These would all be influenced by external characteristics of the individual and the environment. Overall QoL would be the individuals perceived satisfaction with their life once they have taken their symptom status, functional status and general health perceptions into account [89].

This model was the first of its kind and it led clinicians to recognise the holistic management of their patients as their function and overall HRQoL could be altered by addressing any combination of the levels or individual and environmental characteristics. This was a departure from simply treating the disease or the symptoms thereof [89], [90].

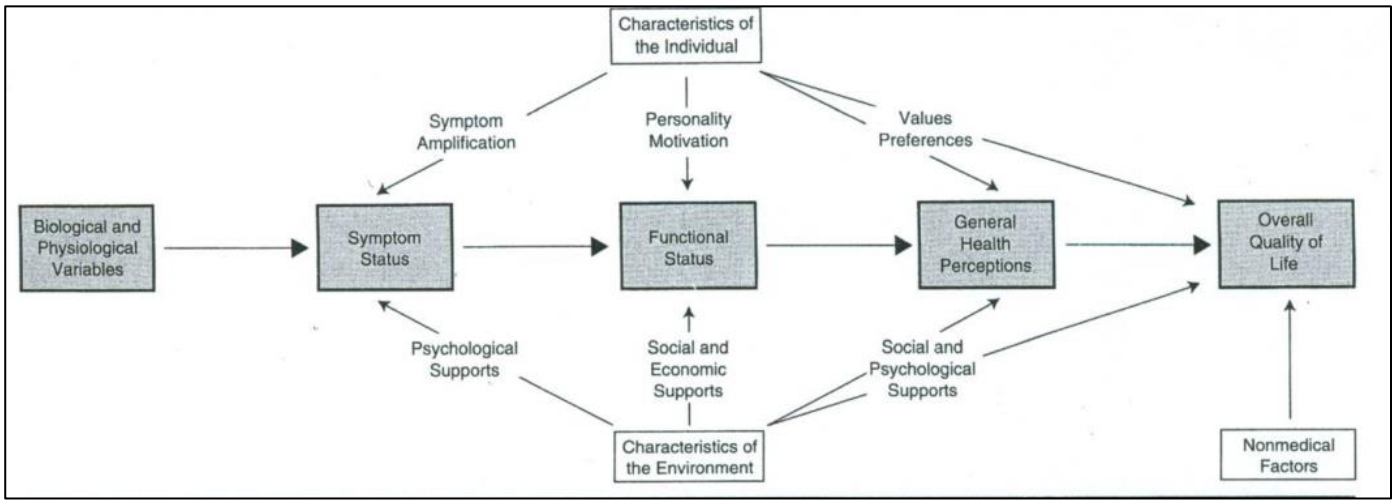


Figure 2-1 Wilson and Cleary Model of Health-Related Quality of Life

Figure 2-1 *From: Wilson, I. & Cleary, P., 1995. Linking Clinical Variables with Health-Related Quality of Life. A conceptual Model of Patient Outcomes. Journal of American Medical Association, 273(1), pp.58–65. Page 60.*

Adapted Wilson and Cleary Model

The Wilson and Cleary Model of HRQoL was revised by Ferrans et al (2005), with the aim of increasing its use and relevance in nursing and health care [91]. Two years of research revealed the importance of the characteristics of the individual and environment on the outcome of all of the levels of functioning [91]. The model was thus revised to include arrows between characteristics of the individual and environment to biological function (Figure 2-2). In addition to this change, nonmedical factors were also excluded from the

adapted model. The inclusion of nonmedical factors as a separate influence on HRQoL was criticised as factors were thought to already be included in characteristics of individual or environment. The adapted model further excluded the examples under the characteristics of the environment or individual, as these were thought to be prescriptive in defining the relationship. The direction of the arrows was excluded from the adapted model as they were thought to further label the relationships between levels of functioning and the interaction with the individual and the environment (Figure 2-2) [91].

The adaptations made by Ferrans et al (2005), were thought to improve the model and increase its scope by expanding on the individual and environmental factors [90]. If one relates this model to an existing HRQoL measure such as the EQ-5D-Y, the measure of symptoms and functional status is achieved through the five dimensions (mobility, looking after myself, usual activities, pain or discomfort and worried, sad or unhappy) rated on a Likert Scale. General Health perception is captured on the EQ-5D-Y on the general rating of health on the VAS.

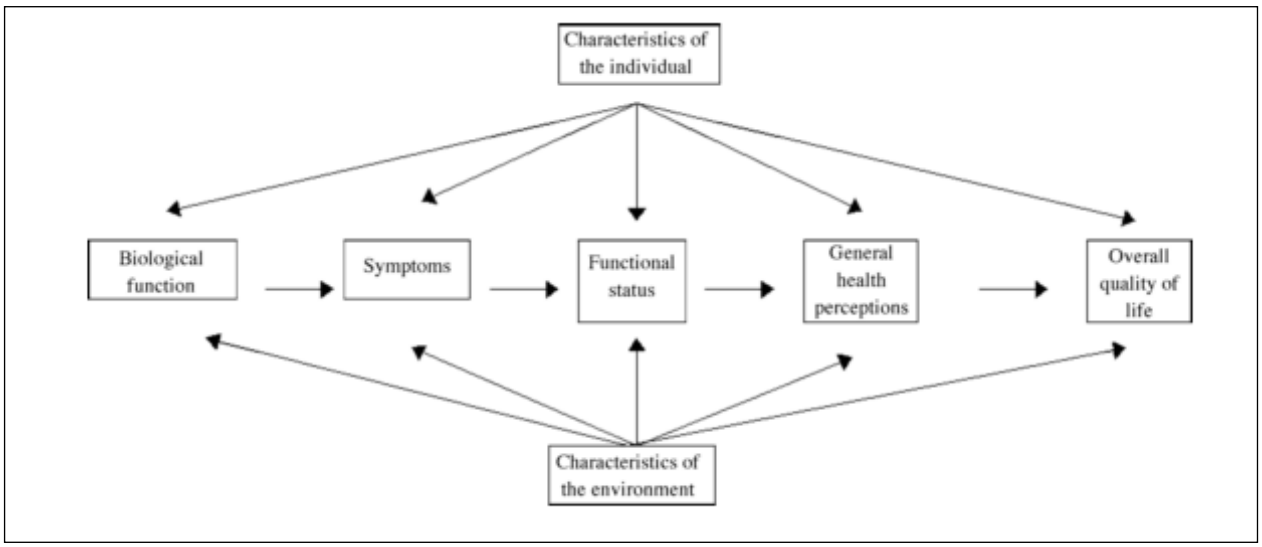


Figure 2-2: Revised Wilson and Cleary Model for Health-Related Quality of Life

Figure 2-2 From: Ferrans, C.E. et al., 2005. Conceptual model of health-related quality of life. *Journal of Nursing Scholarship*, 37(4), pp.336–342. Page 338. Used with permission from Ferrans, C.E.

Taylor Model

Liver transplantation is becoming available to more children with improved medical outcome and survival. The psychosocial consequences after transplantation and the gruelling recovery period are under investigation. Thus, Taylor et al (2009), set out to identify the factors affecting HRQoL after liver transplantation in adolescents, with a specific interest in assessing the influence of transplant-related, personal and family-related variables on HRQoL [77]. The model proposed by Taylor et al (2009), was the

first of its kind to try and summarise the difference in HRQoL for adolescents post liver transplantation [77]. The model was very similar to that proposed by Wilson and Cleary in that it considered biological function and symptoms, in terms of transplant related variables, as well as characteristics of the individual and the environment, in terms of young person related variables. These were thought to affect the overall HRQoL which took into account physical, psychological and social function. This model however included two unique factors: the development of the adolescent over time and consideration for the future [77]. This was perhaps a characteristic which was thought to be unique to children and adolescents as their future arguably holds more value. Although there is no published literature on the topic, a discussion at the 2nd EuroQoL Academy Meeting in Noordwijk, March 2017, revealed that future or future capacity was found to be one of the determinants of HRQoL during the initial qualitative work done on the development of the adult EQ-5D-3L [92].

2.3.2.4 Functioning

The ability to function and perform one's everyday activities was identified in Section 2.3.2.1 as being interrelated with health, well-being and QoL. In addition, functional status is included as a contributor to HRQoL within the models of HRQoL described above. The International Classification of Functioning Disability and Health (ICF) is considered the gold standard for classifying function and was endorsed by the WHO in 2001 [93]. The classification includes all of the positive aspects of function namely: body structure and function, activity and participation and it takes into account both the environmental- and personal-factors of function. In contrast disability encompasses the negative aspects of function: impairment, activity limitation and participation restriction (Figure 2-3). The ICF model takes into account the interplay between the different areas which are affected by health condition.

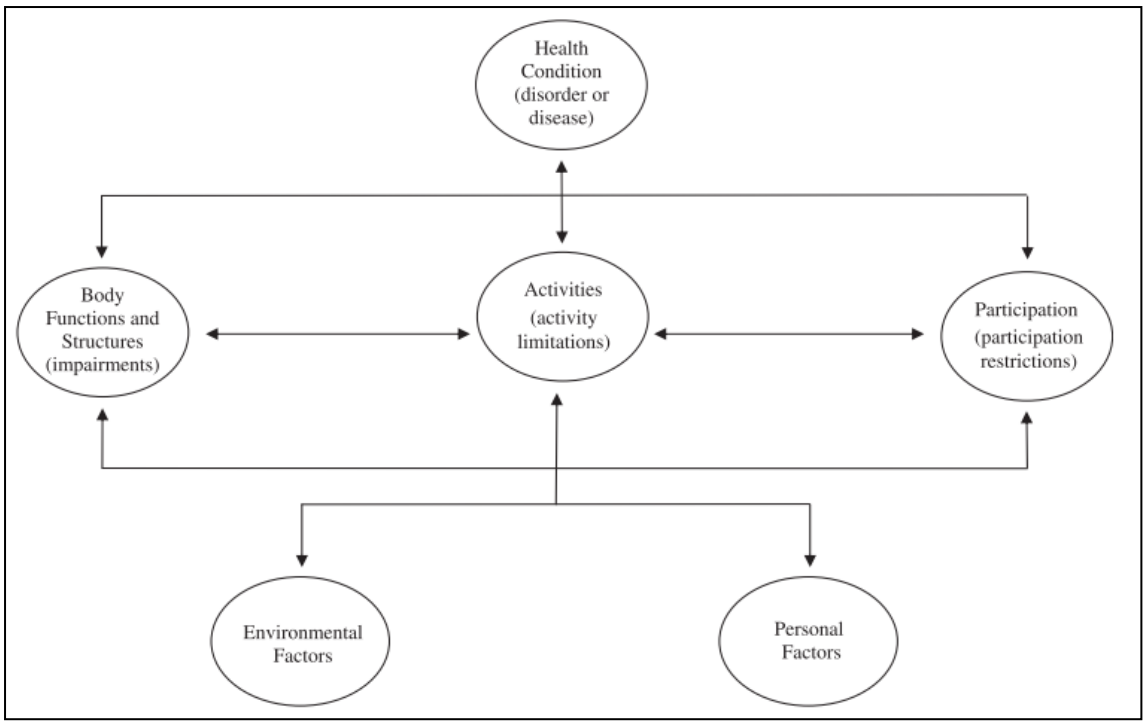


Figure 2-3 International Classification of Functioning, Disability and Health

Figure 2-3 *From: McDougall, J., Wright, V. & Rosenbaum, P., 2010. The ICF model of functioning and disability: incorporating quality of life and human development. Developmental neurorehabilitation, 13(3), pp.204–11. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20450470. Page 205.*

Although the ICF claims to present a holistic conceptual framework limitations have been identified by different researchers. For example, the interaction of environmental factors in relation to creation of disability is not clearly presented in the framework, as environmental factors may impact on each component of the classification [94]. A literature survey conducted by Jelsma (2009) also revealed various challenges including overlapping of codes, not enough or missing codes to capture all problems [95]. Another difficulty was demonstrated in the use of qualifiers under the activities and participation which hampered, in some conditions, the standardisation of ICF application [95]. A further concern with the ICF is that although it claims to be based on a bio-psychosocial model of health, it remains biased towards the medical model. This is particularly evident in the use of the ICF within clinical and rehabilitation settings which results in an under-valuing of the effect of the environment on functional limitations and participation restrictions. This issue was highlighted in the systematic review of the use of the ICF within clinical and rehabilitation contexts in the Nordic countries by Maribo et al (2016) which concluded that the contextual factors were the least used components [96]. In addition, the development of the core sets, which are targeted at specific disease conditions, undermines the principle of causal neutrality and may further emphasize the impairment and health related aspects of functioning to the detriment of the contextual factors [97].

Functional assessment places the focus on describing and measuring a child's abilities and the limitations in function when carrying out the ADLs which are essential to their needs [28], [47], [57]. This would include all determinants of function including; physical, social, cognitive and emotional. Functional assessment further takes into account the use of specialised equipment or assistive devices which are utilised in carrying out the function. Thus independent mobility would be scored equally for children who have independent ambulation with a walker or wheelchair [57]. Two commonly used functional assessment measures available for children include the Pediatric Evaluation of Disability Instrument (PEDI) [98] and the Functional Independence Measure for Children (WeeFim) [57], [99]. They can be scored by an observer or through interview with the caregiver [57].

Of more relevance to our topic, McDougall et al (2010), have criticized the ICF Classification system as it does not incorporate any aspect of QoL or HRQoL [100]. As pointed out by Cieza et al (2005), HRQOL and ICF represent two different perspectives from which to look at functioning and health, a model which encompass both perspectives would be useful [101] . Such a model was proposed that included HRQoL as an all-encompassing sphere around the current ICF model [100]. The WHO suggested that HRQoL comprises of four core life dimensions: physical, psychological, social relationships and environmental [2], [100]. The ICF included these dimensions within their model as the components of functioning and contextual factors which could be viewed as the results of an individual's HRQoL. McDougall, Wright and Rosenbaum (2010), reviewed the ICF model as a proposed model for HRQoL and proposed that the model include an individual's HRQoL which is a dynamic phenomenon as a result of all of the aspects of functioning that may be affected due to an individual's health condition, personal factors and environmental factors [100]. This was to ensure that a holistic assessment of an individual was obtained when considering function. At the time that this model was considered it was suggested that an individual's satisfaction with life and HRQoL be included as codes in the personal factors component of the ICF, which has yet to be implemented [100].

The modified model of the ICF (Figure 2-4) has included an encompassing sphere of human development over time [100]. Development in this model accounts for change which happens, in varying degrees, across the life span from childhood into adulthood. Development is perceived as a variable process which responds to changes in any of the categories defined the ICF and is thus illustrated as a sphere encompassing both the categories of the ICF and QoL The modified ICF model highlights the importance of capabilities and possibilities even more and further detracts from the negative aspects of disease and impairment [100].

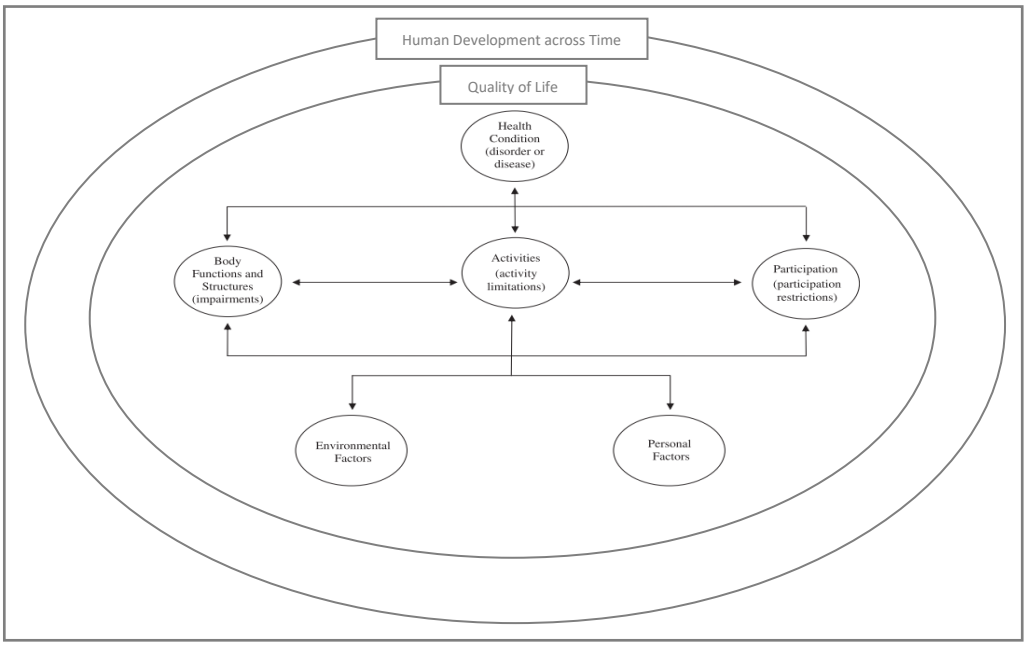


Figure 2-4 Adapted International Classification of Functioning, Disability and Health

Figure 2-4 *From: McDougall, J., Wright, V. & Rosenbaum, P., 2010. The ICF model of functioning and disability: incorporating quality of life and human development. Developmental neurorehabilitation, 13(3), pp.204–11. Page 208.*

Many researchers have compared existing measures of HRQoL to the ICF model in order to support claims of content validity in the HRQoL measure [3], [93], [100], [102]–[104]. Several of the measures including, the EQ-5D and EQ-5D-Y, have been criticized for having most of the items in the area of body functions and activities and none in environmental. [100] [3]. Furthermore, when the EQ-5D was mapped to the ICF there was a concern that the specificity for function or activity was not reflected in the measure [100] [3]. This could lead to ambiguity in the response to these items. For example the item 'walking about' was mapped to one code on the ICF however, the ICF contains more specific codes for walking short distances, long distances, over different surfaces etc. Thus, reporting no problems on the EQ-5D may not necessarily translate into no problems in all of those areas [100] [3]. It is however important to note that generic HRQoL measures may be measuring a far more general construct of health rather than looking at the specific level of deficit in activities or participation as recorded using the ICF. This is evident in that the ICF

maps and details every aspect of disability [104], [105] whereas HRQoL measures produce a more global assessment of health on an ordinal scale [106].

2.3.2.5 Theories/Models of Child Development

The WHO constitution (2006) highlights the important of health and states that the "healthy development" of children is rudimentary and this is dependent on the child's capacity to adapt to a "changing total environment" [46] page 1. The Question is raised as to whether the new instrument should be norm or criterion referenced and if norm referencing is used it is important to know what the norm is. Theories of child development are discussed below as well as the implication of these theories for the measurement of HRQoL in young children.

2.3.2.5.1 Neuro-developmental Trajectory

2.3.2.5.1.1 Development of self-regulation

Developmentally appropriate self-regulation is imperative for the emergence of other developmental tasks [107]. Negative emotions or dysregulation thereof has the potential to disrupt psychological processes too. Emotions arise to co-ordinate and synchronise the body's physiological systems to ensure adaptation or survival in response to environmental changes or opportunities [107]. Emotional regulation develops through experience where one learns to modulate your emotions through internal or operationalised processes. Whereas self-regulation is the process involving control of one's actions in order to achieve a goal [107]. In infancy and early childhood this self-regulation develops through the interaction with the caregiver. As a child gets older they are able to internalize the emotions and regulate their emotions, the strategies developed in childhood carry over into adulthood affecting all dimensions of their emotional regulation [107]. Considering the development of a new instrument to measure HRQoL in very young children, most especially infants, it may be necessary to measure the HRQoL of the caregiver as well as the child due to this intimate interplay allowing for the development of self-regulation. If the caregiver has ill-health or difficulty engaging with the child this may have a spill-over effect on the child's HRQoL which would need to be captured either on the same instrument or on two different instruments [108].

This spill-over effect may be less important in older children as self-regulation typically develops in a child from the age of two years into adulthood [109]. This has been attributed to the cognitive development needed in order to monitor their own behaviour according to the demands of social and non-social circumstances [109]. Kopp (1982), has dedicated much work into exploring the antecedents of self-regulation where cognition is not as developed and has proposed four phases of control [109]. In this early

phase of life the infant is able to modulate their arousal state through reflex movements such as the movement of hand-to-mouth for thumb-finger sucking [109]. Sensorimotor modulation in children between 3-12 months is categorised by the child's ability to perform voluntary motor tasks and change their action in response to an external event [109]. The phase of control, which is evident between 12-18 months shows the ability of the child to recognise and later follow commands defined by the caregiver to social or motor tasks [109]. This phase develops together with the changes in cognitive processing which allows for adaptive responsiveness and problem solving [109]. Self-control emerges when the child is able to delay an act on request and to behave according to expectations, which typically develops around 24 months of age [109].

Emotions may need to be operationalized through self-regulation or the interaction or relationship with the caregiver in a new HRQoL measure. Careful consideration would need to be given to the four phases of control and their respective ages of emergence. It is imperative that this important aspect of emotions are not neglected in the measurement of a very young child's HRQoL but accurately captured by age appropriate items and descriptions. In the period of 0-24 months the development of a child's self-regulation and emotions are directly dependent on that of their primary caregiver. Consideration needs to be given to capturing the HRQoL of the caregiver as well as the child in order to better measure and understand this relationship. Further understanding of motor development is important to ensure the sensitivity of the dimensions or items of physical functioning on a new measure.

2.3.2.5.1.2 Theories of Motor Development

The early neural-maturationist theories from the 1900s postulated the maturation of the central nervous system was as a result of a genetic sequence and resulted in motor development. This development was ordered and began from the head and worked toward the feet and began centrally and moved outwards [110]. This theory was later challenged by the Dynamic Systems Theory which postulated that the environment also had an effect on development. Thus development was a result of the infant's body parts, mood, brain development, environmental conditions and requirements of the task. The changes in any of the conditions would result in changes in the behaviour or development, which may be unstable at first and then evolve into a stable organization of movement [110]. The role of the nervous system became important once again in the Neuronal Group Selection Theory (NGST). Development and behaviour are said to shape the nervous system into dynamic networks according to the structure and function of different tasks. NGST takes into account the interaction between both genetic and the environment [110].

The theories of motor development attempt to provide an explanation for the rapid acquisition of skills during this time. Childhood is characterised by a number of 'normal milestones' for gross motor development, fine motor development, communication and cognition. The younger the age of the child the more rapid the development of these skills [111], [112]. There are globally accepted milestones which a child should reach, for example the ability to walk between the ages of 12-18 months. The age bands are not prescriptive as one needs to take into account the variation between children and their cultural and environmental influences [110].

Measuring HRQoL over a wide age-range may prove challenging due to this rapid acquisition of skills. In older children physical functioning such as mobility is easily measured at the highest functional level of walking. For developing children this is more of a challenge as mobility progresses from rolling, sitting, crawling, cruising and then to walking. Thus the age range for inclusion on a measure for very young children will need very careful consideration. Alternatively items will need to be worded in a manner to assess general abilities rather than age specific abilities. If items or dimensions are used over a larger age band of children careful attention will need to be given to whether the item measures an equivalent construct across different ages.

2.3.2.5.2 Psychoanalytical Theories

2.3.2.5.2.1 Erik Erikson's model of psychosocial development

Erikson was the pioneer in developing a theoretical framework identifying the stages of identity formation. The model is based on overcoming conflicts during different life stages taking into account social constructs, culture and ethical behaviour. Erikson's Model comprises of eight stages ranging from birth to late adult hood. The first three stages (applicable to childhood) are described [113].

Erikson's first stage of basic trust versus mistrust is apparent in children from birth to 12 months of age. This stage is described by the interaction of the child with the caregiver which allows for a reciprocal relationship where their needs are met by their caregiver. This stage is important in that it shapes the child's identity [113]. Autonomy versus shame and doubt is the second stage and is seen in children aged 12 months to 3 years when they begin exploring their environment and they have learned to discriminate themselves from others. Furthermore, they master control of their body and caregiver control is vital in not instilling any doubt or shame when they don't achieve tasks such as toilet training [113]. The third and final stage of early childhood (3-6 years) is defined by initiative versus guilt. Most children start pre-school during this period and start to explore and play with other children of a similar age. During this stage they learn accountability [113].

Erikson's Model is important when considering items which would fall under the broader dimension of social functioning. Similar to the development of self-regulation [107] Erikson's first stage is rooted in the interaction between caregiver and child and from aged 12 months they are less dependent on this interaction. This model is important in defining social interactions with family, peers and within the wider community. Social interactions would need to be further considered together with theories of attachment which explains the development of relationships.

2.3.2.5.2.2 Theories of Attachment

Bowlby build on Freud's model of close relationships with his model which emphasized the role of close relationships [114]. He was also interested in the concepts of regulating internal states, relationship experience as well as communication and exploration across a distance from the caregiver. Bowlby described four stages of attachment. The first stage develops in infants aged 0-2 months are in a pre-attachment stage characterized by crying, smiling, babbling, grasping, reaching, tackling, listening, responding. This corresponds directly to the period of pre-verbal communication [115]–[118]. Bonding is the relationship that the caregiver forms with the child whereas attachment is what the infant forms in response to the caregiver or to the reactions to the caregiver. The second stage is attachment development and occurs from 3-6 months. Clear-cut attachment develops from 7 months to 3 years so there is clear stranger anxiety. From the age of 3+ there is goal corrected attachment where they enter into a more complex relationship with caregiver [114].

Mary Ainsworth developed the strange situation procedure (SSP) and she describes 3 normal attachment types: secure attachment, insecure-avoidant, insecure-anxious attached. The fourth attachment type, disorganized is associated with psychopathology. In the young child disorganized attachment could be characterized by unexplained difficulty feeding and sleeping as well as inconsolable screaming [119]. Difficulty with feeding and sleeping are complex items to consider in young children but would need to be considered due to their link with dimensions of both physical and psychological functioning defined by HRQoL. Problems with feeding and sleeping may be considered prevalent problems in childhood but can similarly indicate notable health concerns. Similarly inconsolable screaming could indicate physical, psychological or social dysfunctioning which would need attention in any child.

From the perspective of developmental and psychoanalytical theories it would be advised that one should not measure the HRQoL of a young child without taking the caregivers' HRQoL into account due to the development of self-regulation, bonding and attachment. The rapid development and acquisition of skills during the first three years of life needs to be taken into account when considering the age range for a new

measure. Furthermore the equivalence of items or dimensions across age groups would need to be evaluated. These theories further show how very important the first years of life are for shaping what we become as an adult. These stages can be disrupted very easily by negative experiences due to the determinants of health. All of these theories are of importance individually but when considered in light of each other it forms an important guideline into the holistic development of the child. These theories should thus be considered as an over-arching guideline for the consideration of descriptors of items and dimensions of the new measure. Although these theories would be useful to consider in conjunction with conceptual frameworks of HRQoL or function they cannot stand alone when considering the development of a new measure. Furthermore, the role of the new HRQoL measure would need to be clarified when developing a new measure.

2.3.2.6 Conclusions Regarding a Conceptual Model

The Wilson and Cleary Model is the oldest and most cited model [90]. It was ground-breaking in its time as it was the first model to emphasise the fact that an individual's values and preferences affect overall HRQoL, which now forms part of the accepted definition of HRQoL [91]. This is included as the basis of development of the subsequent models. The four models discussed have similarities in that they take into account the importance that personal factors and the environment make in the relationship between these key areas [77], [90], [91], [100], [120], they all take into account the presence or absence of disease or a health condition [77], [91], [100], [120] and they all include aspects of physical functioning [77], [91], [100], [120].The unique aspect of development and the future which was introduced in the Taylor Model could be likened to the all-encompassing sphere of development in the adapted ICF Model which would include the future if one considers development as being an ongoing process through the lifespan [77], [100]. Bakas et al (2012), suggest that the ICF may be more applicable across age and cultural groups [90]. The ICF model has however, been criticized as it was not developed as a HRQoL model and thus does not express the same clear defining points of HRQoL as does the Wilson and Cleary Model [90]. The recommendation from the literature review conducted by Bakas et al (2012), was that either the Wilson and Cleary, Adapted Wilson and Cleary Model or the ICF be used when developing a new instrument [90]. The author's preference is however, toward the adapted Wilson and Cleary Model as it includes both the individual and environmental characteristics [90].

For the purpose of developing a new instrument for very young children it was considered important to take into account development across the lifespan. Neither the Wilson and Cleary or adapted models take development into account. This concept was introduced in both the Taylor Model and the adapted ICF Model. The Taylor model is however disease specific and takes into account factors related to adolescents

which are different to that of a young child experiencing rapid development. Although the ICF was developed as a classification system for functioning and disability if one considers the all-encompassing structure of the ICF it could be used as a theoretical structure to ensure that the domains of the new measure can be represented in each of the broader domains of health, body structure or function, activity and participation.

2.3.3 Procedure for Development of a Health-Related Quality of Life Instrument

2.3.3.1 Methodology for Instrument Development

The development of HRQoL instruments have been criticized in the literature for not adequately incorporating a conceptual framework of HRQoL and the perspective of the target population [15], [80], [82]–[84], [121]. HRQoL assessments for children are not exempt from this criticism [4], [83], [122]. In order to provide background to the developmental process of the proposed measure, methodological aspects of questionnaire development will be discussed. Stone (1993), proposed a guideline for the nine essential steps to follow when designing a questionnaire (Figure 2-5) [79].

Designing a Questionnaire:

(1) Decide what data you need

(2) Select items for inclusion

(3) Design individual questions

(4) Compose wording

(5) Design layout

(6) Think about coding

(7) Prepare first draft and pre-test

(8) Pilot and evaluate

Figure 2-5: Steps in Designing a Questionnaire

Figure 2-5 *From: Stone, D.H., 1993. Design a questionnaire. British Medical Journal (Clinical research ed.), 307(6914), pp.1264–12666. Page 265.*

This could be likened to the four phases which were described by Sprangers et al (2003), in developing a series of HRQoL measures for patients with cancer [80]. The first phase was described as generating the relevant QoL questions which could be represented by the first step in Figure 2-5. This comprised of a number of steps including a literature review on HRQoL and existing generic and disease-specific HRQoL measures. Structured interviews with health care providers gathered feedback on the HRQoL questions

identified from the former step. The preliminary list of HRQoL issues and core instrument was administered to the target population for feedback [80]. The second phase of item generation would be equivalent to steps 3-7 (preparing the first draft) in Figure 2-5. This entailed that the final list generated in the first phase was developed into questions with a set format [80]. The third phase of pre-testing the questionnaire would encompass steps 7-8 in Figure 2-5. This entailed administering the questionnaire to a group of patients in the target population by means of a structured interview in order to identify potential problems with administration or questionnaire design [80]. The fourth and final phase of field testing to determine validity, reliability, cross-cultural applicability and acceptability and would be summarised by Step 9 in Figure 2-5 [79], [80].

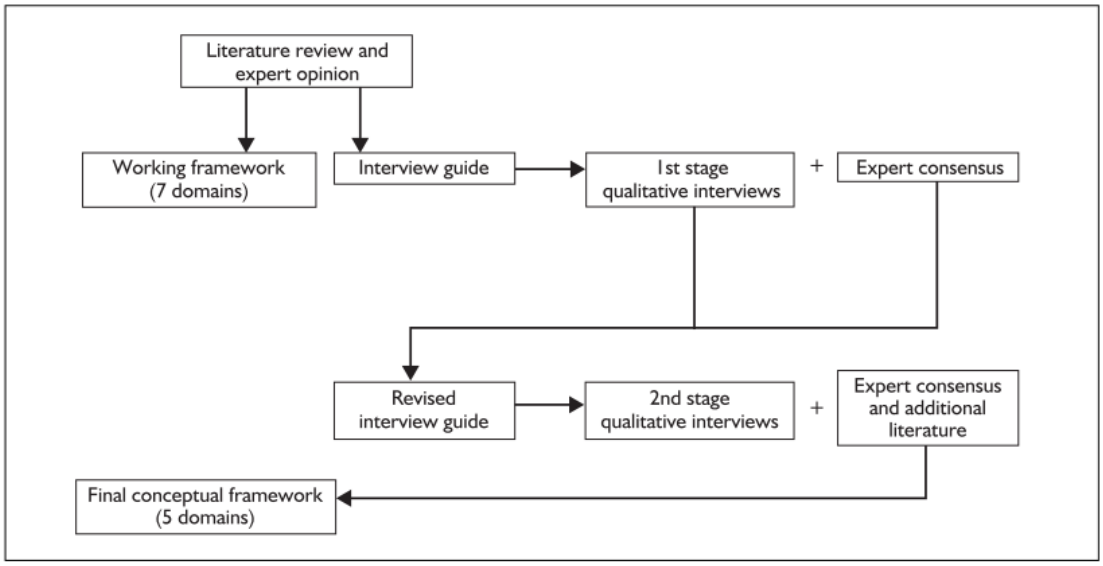


Figure 2-6: Development of the Conceptual Framework of a Proxy HRQoL Measure for People with Dementia

Figure 2-6 From: Smith et al (2005). Measurement of health-related quality of life for people with dementia: development of a new instrument (DEMQoL) and an evaluation of current methodology. Health Technology Assessment. Page 22. Used with Permission from Banerjee, S. (corresponding author).

A similar method was employed by Smith et al (2005), in the development of a proxy measure to evaluate HRQoL in people with dementia and is summarised in Figure 2-6 above [123]. This method makes explicit use of qualitative interviews followed by expert consensus in two stages until the core set of dimensions is developed. It further makes reference to the development process in terms of a broader conceptual framework [123].

The conceptual framework is typically informed by a literature review, expert opinion and patient

perspective as shown in the PROM development process as described by Brod et al [121] in Figure 2-7 below. This model was adopted to ensure that the content validity of the measure was sound and provided further evidence that the conceptual framework, items and measurement approach were derived from the target population in order to fulfil FDA requirements [121].

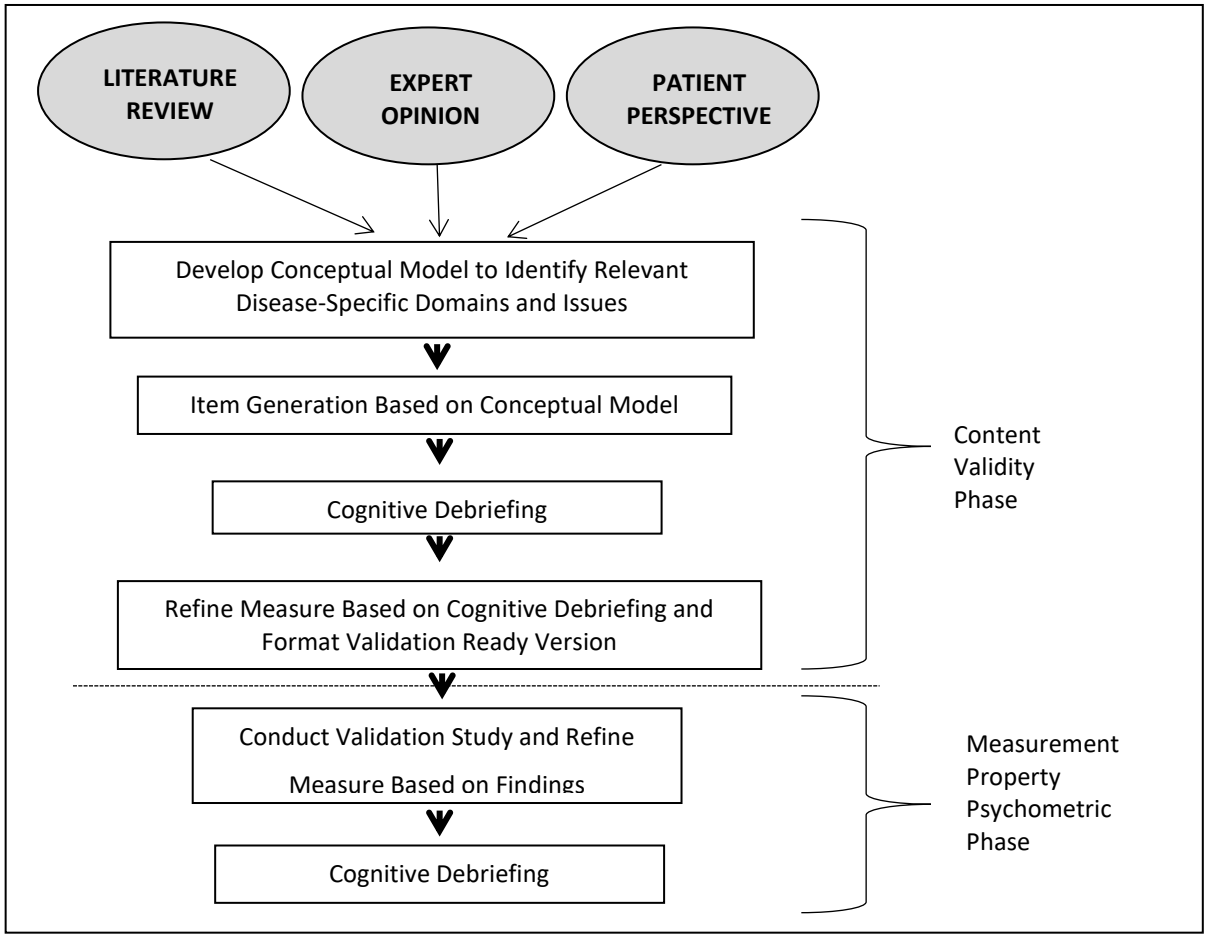


Figure 2-7 The PROM Development Process

Figure 2-7 *From: Brod, M., Tesler, L.E. & Christensen, T.L., 2009. Qualitative Research and Content Validity: Developing Best Practices Based on Science and Experience. Quality of Life Research, 18(9), pp.1263–1278. page 1265. Used with permission from Brod, M.*

It is suggested that qualitative research with the target population is the most appropriate means of data collection to support sound content validity [121]. The process further delineates the process for ensuring content validity for a new measure or an existing measure. When developing a new measure, the content validity should be based on previously identified concepts from literature review or expert opinion and new concepts suggested by the target group during cognitive interviews [121]. In contrast when ensuring content validity for changes to an existing measure one needs to test whether the existing items are relevant to the target group and whether any new concepts need to be included in the measure [121].

Similar processes to HRQoL measurement development are well-described and the development of a conceptual framework is essential to the process [15], [81]–[83]. The conceptual model to be followed for development of a new HRQoL for very young children is discussed further.

Recommended methods for reviewing literature, obtaining expert opinion and patient perspective, conceptual models, instrument development and testing are discussed below.

The methodology employed in each step of the development of the new instrument needs careful attention to ensure content validity [121]. Each of these considerations is discussed below with reference to the literature on different methodology to follow and a conclusion is drawn regarding the methodology that will be employed within the working framework for development of a new measure.

2.3.3.2 Item and Dimension Generation

Content validity is one of the essential requirements for any outcome measure and the process of identification for appropriate items for inclusion needs to be rigorous. The dimensions need to reflect the definition of HRQoL adopted in the framework and represent the core dimensions of physical, emotional and social functioning [78]. These should include dimensions of both body functions and structure, activities and participation in accordance with the ICF [3], [100], [102], [124], [125]. Furthermore, the dimensions need to be developmentally appropriate and should reflect the major tasks of adaptation through the appropriate developmental stages for the age group [34], [83], [126]. Each dimension may consist of a number of items which together describe the dimension of e.g. physical or emotional functioning. Item generation was examined in multiple sources in the methodology reviewed [15], [16], [23], [47], [79]–[84]. The process typically included review of the literature, qualitative interviews with the target population and consensus or feedback from experts [80], [121], [123]. Each of these methods of obtaining data is discussed further.

2.3.3.2.1 Qualitative Methods

The recommendations for the development of PROMs suggest that the perspective of the target population be canvassed [13], [33], [121]. Qualitative research with the target population is further suggested to ensure the content validity of the instrument [121]. It could further assist with an acceptable description of observable behaviour considered for each item as suggested in the FDA guidelines [33]. If a measure is designed for proxy completion for children who are too young to self-report , the target population for the

study would then be the proxy respondent, who is most likely the primary caregiver of the child, due to the intimate knowledge they have of the child [83].

Qualitative research can include individual interviews or focus groups [13], [121], [127]. Individual interviews allows the respondent to give a comprehensive view of the subject from their perspective whereas a focus group recognises a wide range of opinions [121]. Both methods have their advantages and disadvantages and it is recommended that they are used to complement each other where possible [121]. Individual interviews allow the participant an opportunity to discuss their feelings within a private, protected space however, there is a large burden on them as they are the only ones contributing to the discussion [121], [127]. In contrast focus groups allow for the collective discussion around a subject but the information shared is influenced by the dynamic within the group and some individuals may not feel comfortable expressing themselves in this manner and other individuals may at the same time dominate discussion [121]. It brings further logistical considerations of arranging a venue and time appropriate for all participants [121].

Another qualitative method which is often used to augment information from focus groups or to provide unique information is cognitive interviews [13], [127]. There are two methods for conducting cognitive interviews: think-aloud and verbal probing techniques [127]. The think-aloud technique relies on the respondent to verbally express what they are thinking when asked a question. There is little interaction between the interviewer and respondent and the interviewer only probes the respondent for an explanation of their thoughts [127]. The advantages of this technique include the minimisation of bias from the interviewer, the interviewer does not require any training and the format of the interview is open-ended. The disadvantages however, include the fact that the respondents need to be trained in how to express their thoughts verbally; it places a cognitive burden on the respondent and may be subject to bias from the way in which they process information. There is often resistance from the respondent to share their thoughts or there is a tendency of the respondent to lead their thoughts away from the question to be addressed [127].

In contrast the verbal probing technique asks the respondent a specific question which they answer, the interviewer then asks further ‘probing’ questions in order to identify the reasoning behind the response [127]. This method has the advantage in that the interviewer has control of the interview and the respondent does not require any training. The disadvantages include that it could be considered as more artificial than the think-aloud method and has the potential for bias from the interviewer [127]. Probing can be done either through the use of scripted probes, which are developed before the interview, or spontaneous probes, which are constructed during the interview in response to the answer given [127].

Scripted probes have the benefit of being prepared before the interview and allow for a standardized questioning in contrast to the spontaneous probe which is often criticized as being less scientific [127].

2.3.3.2.2 Expert Opinion

Input from experts can be obtained in a number of ways. Qualitative techniques of focus groups or cognitive interviews, as described above, are frequently employed. This however, limits the inclusion of experts to those who are have geographical proximity to the researcher as well as those who are able to schedule time for attendance at either a focus group or cognitive interview. The Delphi process is a possible alternative in that these concerns are minimised [128]–[131].

The Delphi technique is a flexible tool for data collection which can be used to meet a number of objectives including: to develop alternative ideas for consideration; to explore subject matter and determine the reasoning behind decisions made by different role-players; to generate a consensus between the respondents of the Delphi study; and to draw comparisons on views of a subject across a wide range of disciplines [128]–[131]. The methodology employed by the Delphi technique is usually categorised by purposive sampling where Delphi respondents are invited to participate on the bases of the expert knowledge which they can contribute on the subject matter [129]. There are no established guidelines on the size of the expert panel or the method by which experts are selected [128]–[131]. It is recommended that the experts who are invited to participate have a variety of interests related to the subject to ensure the entire range of opinion on the subject is sought [129]. It is further recommended that respondents are able to contribute anonymously and are thus able to both present their ideas and react to the ideas of others without bias [129], [131]. Responses can be weighted according to the ranked importance of the experts or they can be unweighted and each expert is given equal importance in the analysis [129]–[131].

The procedure of the Delphi technique typically consists of multiple rounds [128]–[131]. The first round generates ideas with panellists suggesting relevant issues. A summary is then presented in the next round where further opinions can be gauged or issues can be raised. This process can be repeated as many times as necessary until consensus is reached, the construct under discussion is saturated or the time allocated to the study is limited [128]–[131]. The Delphi technique does not provide definitive answers to a subject, such as would be obtained through a scientific review, it can however provide guidance on the subject matter [128], [129]. Bearing this in mind one needs to pay attention to selection of expert participants, the time frame and number of rounds for study completion to ensure that the response rate is as high as possible and the opinion given includes a wide number of respondents from diverse backgrounds [128], [129].

A Delphi study was found to be feasible in establishing consensus on the content, structure and source of content for the development of the Kidscreen questionnaire [132]. A three-round Delphi Questionnaire was sent via e-mail to 24 experts in QoL measurement across Europe. There was good participation with 20 experts completing all three rounds. They were able to reach consensus on the dimensions for inclusion in the measure, the number of items and completion time for the questionnaire. The literature search only revealed one study which used the Delphi technique in their development process. The majority of the literature did not specify what technique was used to collect and assimilate expert opinion.

2.3.3.3 Instrument Development

After the identification of items for further testing one needs to take into consideration how they will be presented within the final instrument. Careful consideration would need to be given to minimising bias, wording for proxy respondents, the age range, the specified time frame, preferred number of items as well as the format of the questionnaire.

2.3.3.3.1 Minimising Bias

Method Biases can be introduced to an instrument in two ways: from the respondents of the instrument and from the manner in which the instrument was constructed [133]. The introduction of bias is problematic as it may result in measurement error which in turns threatens the validity of the instrument [133].

The most frequent bias introduced by the respondent is: social desirability, acquiescence 'yea and nay saying' and leniency effects [123], [133], [134]. Social desirability bias is considered when the respondent gives the most socially acceptable answer often to put themselves in good light [123], [133]. Acquiescence bias is considered as the inclination of the respondent to agree with the questions or answer them positively [123], [133]. Leniency effect is the inclination of the respondent to rate the abilities of someone they are close to as higher than they should. This could be the case when a caregiver is asked to rate the abilities of their child [133]. Some of these biases can be minimised in the way that the instrument is developed [133].

Instrument development needs to be carefully considered so as to negate respondent bias as well as ensure that method bias is not further introduced through the choice of items, the wording of items, the

format of questions and the framework for the measure [123], [133], [134]. In the same way that the respondent can answer an item in a socially desirable manner one needs to take care that the wording of the item does not frame it as more socially desirable and thus lead to respondent agreeing or rating them highly [133]. Consideration should be given to questions which are positively or negatively worded and if included one should endeavour to include a mixture of both items to minimise acquiescent bias, where the respondent agrees with each question [123], [134]. Minimising the leniency effect for proxy respondents may be achieved by including observed behaviours rather than relying on their subjective rating [123], [133]. Due to the item context effect, where the respondent may be influenced in their responses to an item based on their relation to the other items on the measure, it is suggested that questions relating to emotion be positioned at the end of the instrument [133], [134]. One should endeavour to keep item complexity to a minimum by ensuring that items are easily comprehended, concise and specific. Care should be taken to avoid questions which have two parts and that the words used to not have multiple meanings or are words which are used infrequently. Inclusion of these items might lead to respondents interpreting the meaning of the item differently which will in turn cause random responses [123], [133], [134].

2.3.3.3.2 Proxy Respondents

The use of proxy respondents has been discussed in more details above (2.3.2). Due to the fact that the measure will rely on proxy ratings it is further important to consider the wording of the dimensions to allow for the viewpoint from which the item should be considered. The "proxy-patient viewpoint is intended to elicit substituted judgement, where the proxy projects themselves into the body and mind of the patient" when completing the HRQoL measure [32] page 494. "Proxy-Proxy perspective" in contrast asks the proxy to consider the question from their own point of view [32] page 494. Each perspective provides different information and may be favoured due to the study design [32]. HRQoL measures should state the perspective from which they expect the proxy to respond, without this clarification the respondent will draw their own conclusion on the perspective of the question resulting in error variance. Scott et al (2016), recommended the use of the proxy-proxy perspective with the EQ-5D-Y, as this version indicated higher percentage agreement between proxy-report and child self-report for all dimensions except Worried, Sad or Unhappy [135]. This was attributed to the fact that proxy-proxy perspective is based on the assumption that the respondent can accurately report on the child's HRQoL, whereas proxy-patient perspective makes this assumption and the assumption that the proxy knows the child well enough to know how they would have responded [135].

2.3.3.3.3 Age Range for Inclusion

ISPOR suggests four child/youth age groups to use as a starting point for decision making for PROMs. It is however, recommended that specific age ranges need to be established for each new instrument through cognitive interviews with the target population [13]. The first age group suggested is less than five years and the recommendation is that assessment of HRQoL in this age group be done by an observational measure which is completed by an adult [13]. The age group of 5-7 years would possibly be able to self-report if the instrument is developed in an age-appropriate manner, but due to variable results across measures for self-completion in this age group any new instrument would need to show content validity and good psychometric properties [13]. Instruments designed for self-completion for the age group 8-11 years have shown reliability and validity and child self-report is considered as an option for PROM development. For older children, aged 12-18 years self-report is preferred and should be measured whenever possible [13].

There are however, no guidelines that could be identified on how to further delineate the youngest age-group of less than five years of age for HRQoL measurement. Children under the age of five are generally categorised by developmental periods which include: neonate or new-born infant, infant, toddler and pre-schooler [136], [137]. The WHO defines a new-born infant or neonate as a child under 28 days of age and explains that this is the period where the child is most vulnerable and has the highest risk of dying [138]. A child is considered as an infant from birth until their first birthday and this period is characterised by a dependence on their caregiver to meet their needs [113], [139]. A child is considered a toddler from the day after their first birthday until their third birthday [140]. Children acquire and refine a great number of skills during this period through their exploration of their environment [113]. Children are considered to be pre-schoolers between the ages of 3-5 years this is based on the premise that these are the usually accepted ages for attending pre-school [113]. Pre-schoolers have a large amount of interaction with peers during this stage and learn through exploration and play [113]. The suitability of HRQoL instrument development for any of these delineated developmental ages would need to be supported by results of cognitive interviews with caregivers of the children as well as confirmation from experts in the field [13].

2.3.3.3.4 Time Frame

As the recommendation for assessment for children less than five years of age is through an observational measure with an adult [13], the period of recall about the life of a child has potential to introduce recall bias [79]. The longer the recall period the more one is dependent on memory and the higher the potential that there is subjective or circumstantial overflow in the assessment of the child's HRQoL [79]. The recall

period needs to be considered if the measure is intended for discrimination or prediction as these are both comparing HRQoL at certain points in time [18]. One recall period specified for all questions on the questionnaire is preferred [80]. The simplest time period would be considered as 'today', this would however need to be further guided by evidence from the mapping literature review, Delphi study with experts and cognitive interviews with the target population.

2.3.3.3.5 Number of Items

Both the number of items and the completion time directly influence the acceptability and practicality of the measure in terms of burden of completion; missing values and drop-out or non-compliance with research [141] and the possibility of developing preference based weights [83], [142]. It is suggested that the number of items be as small as possibly while maintaining reliability and content validity and being able to elicit valuable information [16], [23], [47], [79], [80]. A generic HRQoL measure which is amenable to the elicitation of preference weights should have a parsimonious number of items as the greater the number of potential health states the more difficult and expensive it is to develop a preference based measure [83], [142].

2.3.3.3.6 Format of Questionnaire

The format in which the questions are asked would further influence the burden of completion on the respondent [141]. The type and number of response options would further impact on whether the instrument would be amenable to elicitation of preference weights [83], [142]. Thus, consideration needs to be given to formats available to answer questions as well as their utility in a HRQoL instrument.

The two most common question types include: open ended questions and close ended questions [143]. Open ended questions allow respondents to answer the question in the way that they wish, using their own words. In contrast close ended questions allow respondents to select the answer from a set of choices [143]. Analysing answers from open ended questions pose a challenge as they need to be coded into more comparable categories by more than one person. Thus, the time and cost of analysing open-ended answers makes closed-ended questions more appealing [143].

Closed ended questions most often make use of rating scales from which the respondent can choose [143]. The points on a rating scale can either be given a numerical value (such as the Visual Analogue Scale or VAS) or they can be described by statements (Likert scale) [143]. When responding to an item using a VAS the

respondent is asked to specify their agreement along a continuous line usually with end points of 0 and 10 or 100, this value can be treated as numerical data for statistical testing [143]. When responding to an item on a Likert scale respondents usually choose the response option which they agree with the most, these items are treated as ordinal or categorical data [143].

Most HRQoL measures make use of Likert rating scales in order to determine the frequency or quantity of difficulty that the child experiences in that dimension [126]. The EQ-5D stable of instruments utilises a Likert rating scales to measure the dimensions and a VAS rating scale for measuring general health [144], [145]. The inclusion of the response options on the Likert scale should be reflective of the respondents cognitive and emotional development [83]. A higher number of items on the Likert scale, without clear distinction between levels, increases the difficulty of completion. There are currently no clear recommendations on the ideal number of items to be included on a Likert rating scale [80], [143]. The higher the number of response options within each dimension the higher the number of possible health states for economic evaluations. As with the number of items the greater the number of potential health states the more expensive it is to develop a preference based measure [83], [142].

2.3.3.4 Scoring System

Generic health measures can be divided into two categories: health profiles and preference-based measures. Health profiles typically give a separate score for each dimension whereas preference-based measures obtain a single summary index or utility score which reflects the preferences for different health states. [23], [47].

Health profiles scores can be compared across groups for each dimension and thus allow for more general assessment of the effects of various health care programmes on individual dimensions, e.g. on pain or on mobility [146]. Health profiles generally have a score allocated to each dimension and many have a single summary score which allows you to add the dimension scores for a total score [147]. This can be compared to the Misery Index used in the EQ-5D, where the sum of the (unweighted) dimension scores were added together [148], [149]. This method has been criticized on the basis that an ordinal scale has no arithmetic properties and cannot be added together to form a score [150] [126]. In addition, simple addition of dimension scores were not found to be equivalent to utility scores [148], [149].

Some measures convert the ordinal scores to cardinal scores through IRT and Rasch Analysis [151]–[153]. This is considered to be the minimum requirement when assigning a scoring system to a HRQoL measure [154]. IRT attempts to explain the response of a person to an item within a probability model. For example

“if a person has a high ability in a particular field, he or she will probably get an easy item correct ” and “conversely, if a person has a low ability and the item is difficult, he or she will probably get the item wrong” [155] page 4. This model is used to evaluate whether the items included in a measure, with Likert scale responses, are fit for purpose. IRT models the response of each respondent, of a given ability, to each item in the test [155]. The limitation of this is that it looks at how common an item is rather than the impact of the item. For example, pain is a very common impairment and would thus have a lower score, although it can be extremely disabling [155]. The Rasch Model, considered by some to be the simplest form of IRT, is a mathematical model linking the probability of the outcome when one person completes one item to the characteristics of the person and the item [156]. Thus, if a measurement has five items which are thought to measure the functional status of an individual it can provide information about how well those five items measure functional status. It gives information about whether the weighting of those items are equal in giving an overall measure of functional state. It can also help ascertain whether the ability of respondents is equally spaced between response options on the Likert scale for each item. Together this provides important information in deciding whether item scores can simply be added together or whether a scoring algorithm needs to be developed for each item and their corresponding level of report [156].

In preference-based measures, HRQoL is indicated as a single number (utility) along a continuum normally between death (0) and full health (1) (scores less than 0 are possible, reflecting a health state worse than death) [142], [157],[146]. This topic will not be exhaustively reviewed as it is not within the scope of this review. A summary of the terms and methods will however be presented in order to understand the uses and potential benefits of the scoring system.

This method was developed in attempt to develop a cardinal unit to measure different health states, independent of the underlying health condition or the intervention presented and thus allow decision makers to compare the relative value of different health states both before and after intervention [1], [20], [158]. Utility weights can provide a means of comparing alternative medical interventions and the outcome in terms of the burden of the health state and the cost involved [41]. The burden of the health state is is measured by this cardinal unit, the QALY which takes into account quality, in terms of HRQoL utility values, and the quantity, or time spent, in a specific health condition. QALYs are measured on a scale between 0 (death) -1 (full health) where the intervals on the scale are equal and losses or gains on the scale can be aggregated [1], [159]. Utilities and QALYs can be used to inform health economic evaluations [20].
The most common methods of obtaining utility weights include the standard gamble technique (SG) [160]–[162], time trade-off method (TTO) [162], [163], person trade-off (PTO) [36], [164], [165] and discrete choice experiment (DCE) [142], [166].These processes for eliciting utility scores are generally accepted for the calculation of QALYs in the adult population [1], [20], [158]. As mentioned above, the QALY assumes

that one year of life in a health state considered to be perfect is worth one QALY (1 year of life x 1 utility value = 1 QALY) and one year of life lived in a health state which is considered less than perfect is worth less than one [159].

The SG technique requires respondents to choose between remaining in a hypothetical state of ill health for a time period, or choosing an intervention which could either return them to full health or end their life [160]. An example of the technique would be: "subject is asked to choose between two alternatives: alternative 1, the certainty of good health for time t, then (being in) state n-1 for time t, followed by death; and alternative 2, the gamble of good health for time t, followed by use of a hypothetical drug with a probability p of keeping the subject completely asymptomatic for time t, followed by death, and a probability 1 - p of causing immediate death" [161] page 122. SG technique performed in face-to-face interviews is often supplemented by use of a visual aid, often in the form of a probability wheel [162].

The TTO method entails presenting the subject with a scenario and requiring them to trade-off the number of years they are willing to give up to live in full health rather than the disease state. Typically the interview will follow this course: Imagine that you have condition x and have 10 years left to live. You can choose to live the full 10 years in your current health state x, or you can choose to give up some of the years of your life to live for a shorter period of time in full health. The respondent will often be presented with a thermometer or a disc prop which gives an easy graphic presentation to make the decision. For example they will be presented with a line from 1-10 and asked to indicate with a cross on the line the number of years in full health that they think is of equal value to 10 years in health state x. This corresponding number can then be used to calculate QALYs [162], [163].

The Global Burden of Disease methodology determined the disability weights used in calculating DALYS by using the PTO [164], approach to valuing health care programs. Each condition has been given a value between 0 (perfect health) and 1 (death) which is assigned to a year lived with that disability. Groups of health care workers from all regions of the world, who were assumed to have professional experience (rather than personal experience) with disability participated in the original weighting exercise [36]. They were asked two versions of the PTO question, the first asked about prolonging the life of individuals with 22 hypothetical health states versus prolonging life for healthy individuals. The second asked about restoring health in individuals with a hypothetical health state versus extending life for healthy individuals. In both cases the participants determined the `point of indifference', the point at which they were unable to make a choice between the two groups. An example might be being indifferent about saving the lives of 200 people with a specific functional deficit for one year or saving the lives of 100 healthy people for a year. In this case the disability weight would be 0.5 [165]. This method was met with resistance from most

participants who were unwilling to trade-off one group above another and many felt that all groups should be treated equally [167].

DCEs typically comprise of several hypothetical choice sets between which respondents are asked to choose. Each choice is described by a set of attributes and each attribute might take on several levels [166]. The resulting choices are analysed to estimate the contribution of the attributes to overall utility. DCEs facilitate valuation of multiple options rather than evaluating a single intervention or treatment [142], [166]. An example of DCEs would be that a subject is presented with a set of attributes related to a child's health state e.g. pain level, with an appropriate range of attributes e.g. mild, moderate or severe. Two different scenarios are described and the respondent is asked to choose between them. This will typically be done in a series of paired choices in a discrete-choice questionnaire that has been designed to be valid and reliable [142]. The relative importance of each attribute is determined by relating the preferred choices from the repeated choice tasks. An advantage of this is if for example pain and cost were attributes in the method, one could estimate how much the subject is willing to pay for a reduction in the level of pain experienced by the child. If these survey choices are properly structured they can reflect real-life trade-offs that both patients and parents have to face. By including a willingness to pay question in the experiment design, these health and non-health benefits can be combined and utilised in CBA [142].

In considering the conceptual framework in which to develop a new generic measure the benefit of a scale amenable to the elicitation of preference weights has far greater benefits than a scale where the dimension scores are able to be calculated. Thus, a generic measure will be developed which could be amenable to the elicitation of preference weights in the future, although this will fall beyond the scope of this thesis.

2.3.3.5 Pre-Testing of a Newly Designed Instrument

The recommended pre-testing process of the first or Alpha Draft of the questionnaire includes the following procedures. The first draft of the questionnaire should be tested in order to verify comprehensibility, potential bias and appropriateness of dimensions [79], [82], [83], [123], [134]. The preliminary questionnaire is then subjected to psychometric testing to inform further dimension reduction [123]. Psychometric testing should include: evaluation of missing data; frequency of response options for each dimension across the population; presence of ceiling or floor effects (dimensions where the responses favour the high or low end of the scale respectively); reliability of the scale as a whole using Cronbach's alpha as well as inter-item correlation and item-total correlation and factor analysis [123], [134]. The dimensions are then further examined, in terms of whether they are correctly grouped to measure HRQoL. This can be done through establishing the equivalence of item variance (by examining the symmetry of the

item-response distribution), factor analysis (to ensure that items do not load on multiple factors or that they do not load on any of the factors) and whether the dimensions show divergent validity [72], [123], [151], [153], [168], [169]. Dimensions performing poorly across all of these tests are considered for exclusion. IRT and Rasch Analysis could further inform whether the dimensions can be assigned a scoring system [156].

If psychometric testing reveals that dimensions need to be reduced, a Beta Draft of the questionnaire will need to be developed and undergo the same testing. This process will have to be repeated until the final questionnaire is developed and can be tested for validity and reliability [79], [123], [134].

2.3.3.6 Assessing Psychometric Properties of the Newly Developed Instrument

HRQoL can be measured for one or more of three broad purposes: discrimination, evaluation or prediction [18]. Measurement for discrimination is used for cross-sectional analysis for example to determine the burden of disease among groups or individuals at a point in time [18]. Thus, such measures should consistently measure the same construct between different individuals. Measurements for evaluation are used for longitudinal studies and to assess HRQoL within an individual, or groups, over time. Thus, such measures need to be responsive to change within an individual. One may use a HRQoL measure to predict the score on another measure at the same point in time. If the HRQoL measure is shown to be predictive of the other measure you may want to substitute this simpler or shorter measure for a more burdensome measure [18].

Any valid measure irrespective of the purpose of measurement needs to display acceptable psychometric properties if it is to yield useful credible data [9], [10]. To establish whether a new measure is scientifically robust the psychometric properties of reliability and validity need to be proven [15], [141], [145], [170]–[174]. The validity of a measure is an indication of whether the instrument measures what it is intended to measure [15], [23], [123], [141]. The four facets of validity include: face, content, criterion and construct [15], [23], [47], [141]. Face validity is an indication of the extent to which the measure covers the full range of relevant topics, and could be assessed by knowledgeable people within the subject [141]. Content validity is an indication as to whether the dimensions include all items and concepts relevant to the population. Content validity is ensured by including the target population in the development process [141], [175]. Construct Validity is an indication of to what extent the instrument measures the theoretical construct [141]. One can strengthen construct validity through establishing a conceptual framework in which the instrument is developed [15], [23], [47], [123], [175]. Criterion Validity is an indication of the degree to which the instrument yields the same results as an existing validate ‘gold standard’ measure. In

the absence of an established HRQoL measure for comparison one can establish to what extent it discriminates between known groups classified by severity of disease or presence of disease such as TD, AI and CI children [141]. Convergent validity focuses on to what degree measures of the same concept which are theoretically equivalent correlate with each other [141]. This could be established through comparing results from the item of pain on a new measure to an existing validated and reliable measure of pain [145].

The reliability of a measure is the degree to which it yields the same results in repeated measures under the same circumstances [141]. Reliability is often assessed by internal reliability, such as Cronbach's α, which shows agreement between items measuring the same construct [141], [176]. Typically Cronbach's α co-efficient is used, with an accepted standard 0.7 for group comparisons and 0.9-0.95 for individual comparisons [176]. Reliability can further be measured in terms of stability by test-retest in order to establish whether participants give consistent responses over time where the health state is static [15], [141]. Inter-rater reliability indicates that the responses of an individual are consistent between different data collection personnel [15], [141].

2.3.4 Attributes of a Health-Related Quality of Life Measure

2.3.4.1 Generic/Disease Specific Measures

HRQoL measures can be divided into two main categories: disease-specific and generic measures. Each of these approaches has its advantages and disadvantages which alter depending on the purpose of the measurement. In the development of a measure it is important to explain explicitly what the underlying conceptualization is so that future researchers can select their measure according to the objectives of their study [18].

Disease-specific measures are typically developed to measure the effects of a specific disease or condition on HRQoL [23]. Due to the fact that effects on HRQoL can be similar across a number of conditions with similar symptoms the use is often expanded to include other diseases or as a generic measure [16], [61], [76], [177], [178]. Disease-specific measures are argued to be more responsive in that they detect disease-specific clinical changes [16]. This of paramount importance to inform disease management for individual patients [16]. Furthermore, in evaluation of treatment in large cohorts or at individual patient level disease-specific measures will typically be more sensitive to evaluating relevant treatment side-effects [16]. Disease-specific measures are however limited to evaluating HRQoL in the disease that they were developed for and are thus unable to provide comparative data across disease groups or between disease

groups and the general population [16]. Current recommendations include the use of both disease-specific and generic HRQoL measures to evaluate the patient comprehensively [16], [179].

Generic health measures can be used to collect data from both healthy and ill individuals. Generic measures thus have a wider application and can be used in population health surveys, burden of disease studies, epidemiological studies, screening, describing health status, developing management plans for individual patients, informing clinical policy and resource allocation decisions [16]–[22].
Generic health measures can be divided into two categories: health profiles and those that yield preference-based measures. Health profiles typically result in a separate score for each dimension whereas preference-based measures obtain a single summary index or utility score which reflects the preferences for different health states [23]. Some health profile measures, such as the EQ-5D, have values based on valuation studies (also known as disability or utility weights) available and can thus be regarded as preference-based measures. Each combination of health states described by the profile measure is given a preference based value and HRQoL is indicated as a single number along a continuum normally between death (0) and full health (1) (scores less than 0 are possible, reflecting a health state worse than death) [23], [142], [146], [157] . QALYS gained or lost can then be determined by calculating the product of the utility weight and the time spent in this state [159]. Due to the value of HRQoL data in health economics the number of preference-based measures developed for use in children is increasing.

Generic HRQoL measures which are amenable to the elicitation of preference weights will be explored in more detail in this thesis. Although it is not clear whether decision makers would adopt such a measure for health economic decision making in very young children it may prove beneficial in the future. Furthermore, tracking the change in preference weights of individuals across the lifespan may yield important data. Although the elicitation of preference weights does not form part of this thesis it is important to consider the factors which need to be taken into account in developing a new measure to ensure that it is amenable to the elicitation of preference weights if this does arise.

At the time of submission, four measures were identified as available for children or adolescents under the age of 18 years which have preference based values available: Health Utilities Index (HUI) [70], [71], [77]; Child Health Utility 9 Dimension (CHU-9D) [78]–[81] , Adolescent Health Utility Measure (AHUM) [82] and the Assessment of Quality of Life 6 Dimension (AQoL-6D) [83].The EuroQol 5 Dimension Youth version (EQ-5D-Y) is in the process of deriving utilities [39].

In the South African context, a generic HRQoL would have benefits in informing health status across the population, measuring the progress of health technology and services across the country or within an

institution or service, informing policy development and health economic evaluations. Such an instrument should also be parsimonious in items and lend itself to valuation studies. Thus, the focus of this thesis was on generic HRQoL measures which could with time be amenable to the development of preference weights.

2.3.4.2 Self-Report/ Proxy Measurement

By definition, an individual's HRQoL is subjective and should be elicited by self-report whenever possible, even from children [27]. This is not always possibly as there are those who are either too young or cognitively unaware to self-report leaving no choice but to utilise proxy report [16], [27]–[32]. Previously all children were deemed unreliable in answering questions pertaining to their health due to their lack of insight [27]. This has however, changed with the development of a number of valid and reliable self-report measures for children, typically older than eight years of age, such as the EQ-5D-Y [144], Paediatric Quality of Life Measure (PedsQL) [76], [180], [181], Kidscreen [169], [182], [183], KINDL and Kiddy-KINDL [184]. The development of these proxy versions of HRQoL measures has allowed for comparison between self-report and proxy report.

2.3.4.3 Relationship Between Self and Proxy Report in Children's Measures

Eiser and Morse (2001), conducted a systematic review of the relationship between self-report and proxy report for ten HRQoL measures [27]. In general there was good agreement between child self-report and proxy report for dimensions which were more observable, including physical ability and symptoms [27]. Good agreement was reported for physical activity in studies assessing the following: children with chronic illness on the How are you? (HAY?) (r=0.65) [27], children suffering from cancer on the PedsQL (r=0.57) [76] and the Paediatric Cancer Quality of Life Measure (PCQL) (r=0.59) [73]. Agreement for the dimension of physical symptoms on the Perceived Illness Experience (PIE) measure, was also found to be good between proxy and self-report in children with cancer (r=0.84) [185]. Somatic distress as measured on the Behavioural Affective Somatic Experiences Scale (BASES) in children undergoing bone marrow transplantation was found to be good (r=0.57) [186].

In contrast, three studies found poor levels of agreement between raters for physical functioning [27]. The results from the comparison of parent proxy report and child self-report on the Quality of well-being scale for children with Cystic Fibrosis showed poor agreement between parent and child on physical functioning [187]. Langeveld et al (1996), similarly found that there was better correlation between parent and

adolescent for social dimensions than dimensions of physical functioning on the Quality of Life Headache in Youth Questionnaire, designed to measure the HRQoL in adolescents with headaches [188]. A Dutch study of parent-child pairs from schools found that parents and children were least likely to agree about physical complaints when compared to other dimensions measured on TNO-AZL Children's Quality of Life Questionnaire (TACQoL) [35]. Eiser and Morse (2001), further found that there was generally a significant but poor agreement between raters for dimensions which could be considered as social and/or emotional [27]. These dimensions covered a large range of descriptions including: appearance and communication as measured on the PedsQL [76] social functioning as measured on the PCQL; compliance as measured on BASES [186]; and disclosure and impact of treatment as measured on PIE [185].

Results from a subsequent study on the performance of the PedsQL showed that the difference in proxy and child self-report ratings may be attributed not only to dimensions but also to the age of the child and the HRQoL of the caregiver [30]. Similar to results found by Eiser and Morse [27] the PedsQL showed low agreement between dimension scores with low ICC scores (0.02 – 0.23). It is of interest to note that differences between the children's self-report and parent proxy report were largest in the older age group (7.5 – 8.5 years). Conversely there was no difference between parent or child in the youngest age group (5.5 – 6.5 years) [30].

Research has been undertaken to explore the poor agreement between self and proxy report, often referred to as cross-informant variance [16]. Qualitative methods, using the think-aloud technique, were used with parents and children using the Kidscreen to further understand this cross-informant variance [29]. It was found that parents and children use different processes in answering the question. They further interpret some of the words used in the measure differently and base their responses on different reasons or events [29]. Children tended to choose extreme scores (best or worst) and only based their answer on a single event whereas parents considered a number of events/scenarios when answering the question. It was however, found that both parent and child understood the question in the same way [29].

It is further suggested that the cross-informant variance is due to the fact that children may hide their knowledge and impact of disease in order to protect their parents or caregivers [31]. Alternatively they may not want others to know the extent of their suffering or they may not know the potential impact of their disease [31]. Parents or caregivers report may be influenced by the burden of care, their concern for future impact of the disease and their own HRQoL [31].

Proxy ratings often stand alone and are substituted for self-report ratings in children who are too young or too ill to self-report. They can however be used to enhance the information which has been provided in a

child through self-report [16], [27], [31]. The cross-informant variance is not necessarily a negative aspect of proxy report; but one which needs to be noted during evaluation of HRQoL [16], [27], [29]. It is suggested that instead of favouring one form of reporting above another one rather attempts to understand the value behind the data each of the respondents provides [31]. The measurement of HRQoL from both the child and parent point of view can add value to decision making and planning within a family-centred approach to care [31], [189]. One is unable to report on the cross-informant variance for those who are too young or ill to self-report. This is where proxy rating is required and the parent/caregiver /medical personnel need to make informed decisions on the child's behalf [31].

Medical personnel proxies have been found to report fewer problems in HRQoL than parents or patients [27]. Thus, when considering paediatric research proxy measurement parents may provide more useful information than other proxies as they typically have valuable understanding of their child [189]. It may be important to include measurement from the primary caregiver, for example in some cultures grandparents may be more involved in caring for the child [27].

2.3.4.4 Proxy Versus Observational Measures

The FDA and ISPOR guidelines suggest that proxy-measures for HRQoL be based on observable measures [13], [33]. There are broadly two types of informant report questionnaires: proxy measures, i.e. based on an assessment of the subjective experience of the child and observational measures requiring the respondent to base their assessment of HRQoL on observed behaviour [13]. Proxy measures are considered to comprise of items requiring the respondent to interpret the question and thus making a conclusion about the child's subjective experience. An observational measure requires that each item is assessed according to observable behaviour of the child without the respondent interpreting the question or drawing a conclusion [13].

Observational assessment can be achieved in three broad ways: The observational assessment is completed while directly observing the child. This would be similar to the completion of a developmental assessment such as the Bayley Scales of Infant and Toddler Developmental Assessment, which should be carried out by a clinician with professional training in completion of the measure [190]. It consists of 205 items which need to be scored through observing the child attempting the task. Such a method is time consuming, as the Bayley Scales can take up to 90 minutes to complete [190].

The second method requires the respondent to score the child according to what they have heard the child to have said over the specified time period. This would not include the respondent asking the child specific

questions around the HRQoL questions but rather a recall of what may or may not have been communicated [13]. This takes less time to administer and does not require training. It does however, require the child to be verbal and have the cognitive ability to express themselves as it does not allow the respondent to draw conclusions from behaviours that have been observed [13].

The third option would be a general observation of the child's behaviour. This would include items which assess the respondent's general observation of the child's behaviour within the environment(s) the child had been for the specified time period. This behaviour would not be according to a pre-selected list of criteria as with a developmental assessment but a recall of the child's general behaviour over the time period specified by the measure e.g. the last week or today. This would also be easier to administer and would not require training. This has the advantage that it could be done on a child of any age, with or without verbal or cognitive competence [13].

2.3.4.5 Interaction between Proxy and Child Health-Related Quality of Life

The concern with proxy report from a subjective or observational point of view is that one is unable to control for the emotional overflow from the respondent when rating the child's HRQoL. This is a specific concern in caregivers of children with special needs or chronic conditions as it has been shown that it affects the health, emotional well-being and HRQoL of caregivers as well as family functioning [191], [192]. It is difficult to separate the respondent or parent's own experience from the child's health condition and the impact that it has had on them personally. This is often more difficult for the parent or primary caregiver due to the dependency which is integral to their relationship [192]. The extent of these spill-over effects from the respondent is not well-documented and varies by the child's condition and the relationship between respondent and the child. They are however, important to consider for paediatric decision making and potential health economic evaluations and cost-effectiveness as there may be an added societal benefit to medical interventions [108], [192]. The health economic guidelines instituted by NICE and the Dental and Pharmaceutical Benefits Agency in Sweden state that analysis should consider the family [193]. It has been shown in theory that one cannot measure the effects of medical interventions from a societal perspective without considering the life and family situation of the individual in question due to the negative or positive spill-over effects treatment may have on the family [193]. The HRQoL of both caregiver or family and the child should be assessed if the spill-over effect is to be measured it is however, not clear whether the HRQoL of the child and caregiver or family should be assessed using separate instrument or whether preference weights should be developed separately and how this would impact CUA [193]. In the absence of any established guidelines it would be beneficial to measure the HRQoL on an adult preference

based measure and establish the relationship between the respondent and their proxy report of their child's HRQoL.

2.3.4.6 Conclusions Regarding Proxy Response

Ultimately the caregiver's perspective is important as they are often making health care decisions for the child [13] and, obviously in younger children and infants, there is no other option but proxy report. Although there is a concern with the validity of proxy report with regard to it being a true reflection of the subjective experience of the child, there is evidence of generally significant correlations between the two, increasing in younger children. However, to counter the generally low correlations, literature supports the FDA recommendation that observational items should be included in any new HRQoL instrument that will primarily be used by proxy report [33]. The best model to use would be that the respondent reports on the behaviour of the child within a given time period. The development of the measure for the child would need to ensure that the behaviours evaluated by the respondent are developmentally appropriate. Furthermore, consideration needs to be given to the purpose of the measure as well as the psychometric properties of a new measure.

2.4 Conclusion

Measurement of HRQoL of the very young child is important as they suffer the highest burden of disease most notably in LIC and LMIC [5], [87]. A preference-based measure could evaluate the cost and impact of new health interventions implemented to decrease mortality and morbidity [16], [19]–[22].

It was concluded that there was a need for a generic measure of HRQoL for this very young age group to be developed and that this measure should be developed according to the definition of HRQoL adopted from Bradlyn (1996) : "(HR)QoL includes, but is not limited to the social, physical and emotional functioning of the child and adolescent, and when indicated, his/her family, and it must be sensitive to the changes that occur throughout development" [78] page 1334. This was incorporated within a conceptual framework of the adapted ICF model which also takes into account the developmental trajectory of the child [100]. The conceptual framework would further ensure that the dimensions were developed holistically and were representative of body structure and function; activity and participation [100]. The Working Framework will guide the development of the new instrument to ensure content validity. Generation of the item bank and descriptors would be through a mapping review of the literature of existing HRQoL for young children; cognitive interviews with the target group (caregivers of young children) and a Delphi study with experts in

the field [79], [80], [82], [123], [175]. The instrument development would pay careful consideration to the wording and layout of the measure as to minimise bias [123], [134]. Items would be based as far as possible on observable behaviour as recommended by the FDA [33]. The proxy-proxy viewpoint would be used for the wording of all items and instructions on the completion of the instrument would clearly specify the viewpoint for completion [32]. The time frame would be short [18], [79], [80], the number of items brief [23], [79], [80] and a Likert-response scale utilised [80], [83], [126], [143]. The inclusion of these items would all be further guided by the results of the mapping review of the literature, cognitive interviews with the target population and opinion from experts in the field. The development of utility weights would not be developed as part of this thesis but a generic measure will be developed which is amenable to elicitation of preference weights in the future.

The first (alpha) draft of the instrument would need to be pre-tested to ensure comprehensibility, potential bias and item reduction [123]. Necessary changes would be made and the subsequent drafts would undergo similar pre-testing. This process would be repeated until a satisfactory draft is developed for validity and reliability testing [15], [141], [145], [170]–[174].

3 Chapter 3: Mapping Review of Generic Health-Related Quality of Life Measures for Children Under the Age of Seven Years

3.1 Introduction

There is a large body of literature related to the measurement of HRQoL and a large number of generic and disease specific measures have been developed to monitor changes in adults. It is equally necessary to monitor HRQoL in children as both ill health and psychosocial problems in early childhood may have a profound effect on health, behaviour and scholastic achievement in later childhood and adulthood [194]–[196].

A mapping review was undertaken to identify and critique measures which have been developed and validated to measure HRQoL in children seven years of age or younger. The aim was to identify deficiencies of existing measures to inform the development of an appropriate instrument, if a need to develop such a new measure was identified. The variables considered in the review are based on those discussed in the narrative review (2.3.3), and include description of measure development, completion by self/proxy, descriptive dimensions, number of items, response options, frame of reference, recall period, scoring system and psychometric results pertaining to validation, reliability and practicality.

The overall aim of the review was to determine whether there was a need to develop a new measure of HRQoL for younger children in South Africa. The specific objectives were:

- To identify whether there was a suitable HRQoL measure on which to model a new measure, based on:
    - The rigour of the development procedure and applicability across cultural groups
    - Observable dimensions
    - Recall Period
    - Number of items
    - Practicality
    - Scoring System
    - Acceptable Psychometric Properties
- To identify the age group where a new HRQoL measures was most needed
- To identify a bank of items to be considered during the development of a new measure

3.2 Methodology

A mapping review was conducted to analyse the literature, identify important characteristics and gaps in the literature [41]. A mapping review was undertaken as it allows "the contextualization of in-depth systematic literature reviews within broader literature and identification of gaps in the evidence base" [41] page 26. It further allowed the analysis of existing measures according to a *priori* of criteria [41]. The scope of the review was delineated by the researcher and supported by two experts in the HRQoL research field. The search strategy was identified by a task group of three individuals including a HRQoL research expert, a systematic review expert and a paediatric physiotherapist.

3.2.1 Search Strategy

A search strategy for use on electronic databases was developed based on previously published literature as well as expert knowledge from the task group. The only limit to the searches was the inclusion of English articles or abstracts. Articles were searched in each database from the beginning of each database until April 2017. No limits were set regarding earlier dates of articles as important information could have been missed if excluded. Suitable academic books were used. Pearling, which entails using the literature at hand to identify additional relevant studies, was done by hand searching the references of sourced papers. Pearling further ensured that measures which were previously used as disease-specific measures but now have a wider audience were included as well as other articles which did not necessarily include the specified search terms as with generic or relating to children. The websites of identified measures were also consulted for additional manuals or reference papers. The following electronic databases were searched: PubMed, EMBASE, Web of Science, PEDro, EBSCOHost, Africa-wide, NiPAD, CINAHL, ERIC, Health Source- Nursing/academic edition, MEDLINE, PsycARTICLES and PsycINFO, Scopus, Academic Search Premier. Conference proceedings from ISPOR and ISOQoL for the years 2012, 2013 and 2014 were searched for relevant literature. The terms in the title ("Health-Related Quality of Life", OR "Quality of Life" OR "well-being" OR "health status") AND ("children" OR "paediatric" OR "pediatric" OR "infant*" OR "child*") AND ("questionnaire" OR "instrument" OR "measur*") AND "generic" AND ("validation" OR "develop*") were used to identify articles.

3.2.2 Inclusion and Exclusion Criteria

Self-report and proxy report generic measures of HRQoL, health status and wellbeing were included. Measures were excluded if: they were disease specific, their dimensions were restricted to demographic or

environmental indicators, and they only measured a single dimension or were used in children over the age of seven years.

3.2.3 Data Analysis

A data abstraction form was used to record the literature reviewed. Information was gathered on bibliographic details, description of instrument development, completion by self/proxy, descriptive dimensions, number of items, response options, reference of the question to the child's normal behaviour or the behaviour of others, recall period, preference based and psychometric results pertaining to validation, reliability and practicality. Particular attention was paid as to whether the items related to observable behaviour, if this was defined and whether developmental changes were factored into the measures.

3.2.3.1 A Priori for selection of HRQoL measure on which to model a new measure

- The dimensions or items included on the measure should be observable as per the ISPOR [13] and FDA guidelines [33].
- The recall period should be short to eliminate recall bias [79][52] as young children have increased lability due to their rapid development [197].
- Content validity needs to be sound and based on a transparent development process with a variety of stakeholders most especially including parents or children [79], [123], [175]. Development including a variety of cultural groups would be beneficial.
- The measure needs to have a scoring system [23], [47] preferably derived from IRT or Rasch Analysis [151]–[153] or preference based scoring [20], [158], [198].
- Sound psychometric properties in term of validity and reliability [15], [141], [145], [170]–[174].
- Practicality in terms of cost of the instrument as well as personnel costs in terms of length of time to administer or complete the instrument which would be directly related to the number of items on the measure [16], [23], [47], [79], [80], [141].
- As the new measure will be developed in South Africa evidence of cultural validity of the instrument will be preferred.

3.3 Results

3.3.1 Search Outcome

The literature search identified 354 articles of which 59 were duplicates and subsequently removed. JV screened all 295 of the identified research papers. After review of the titles and abstracts 175 of the articles were excluded as they were research articles related to a specific disease, a further 62 were excluded as they were not within the specified age range. An additional 14 articles were excluded based on other criteria. Other criteria included if they were restricted to demographic or environmental indicators, and they only measured a single dimension as per the exclusion criteria. The remaining 39 articles were included in this review. The researcher identified a further 17 articles through manually searching the bibliographies of the included studies (pearling). An additional 17 studies were identified and included in analysis (Figure 3-1).

Sixteen generic HRQoL measures were identified from 57 papers. After consultation with the authors of the Health Utilities Index (HUI), the HUI: 2 and HUI: 3 were categorised as one measure as it is recommended that they are used together. Thus, the reporting of the results will focus on the development and psychometric rigour of the fifteen included measures.

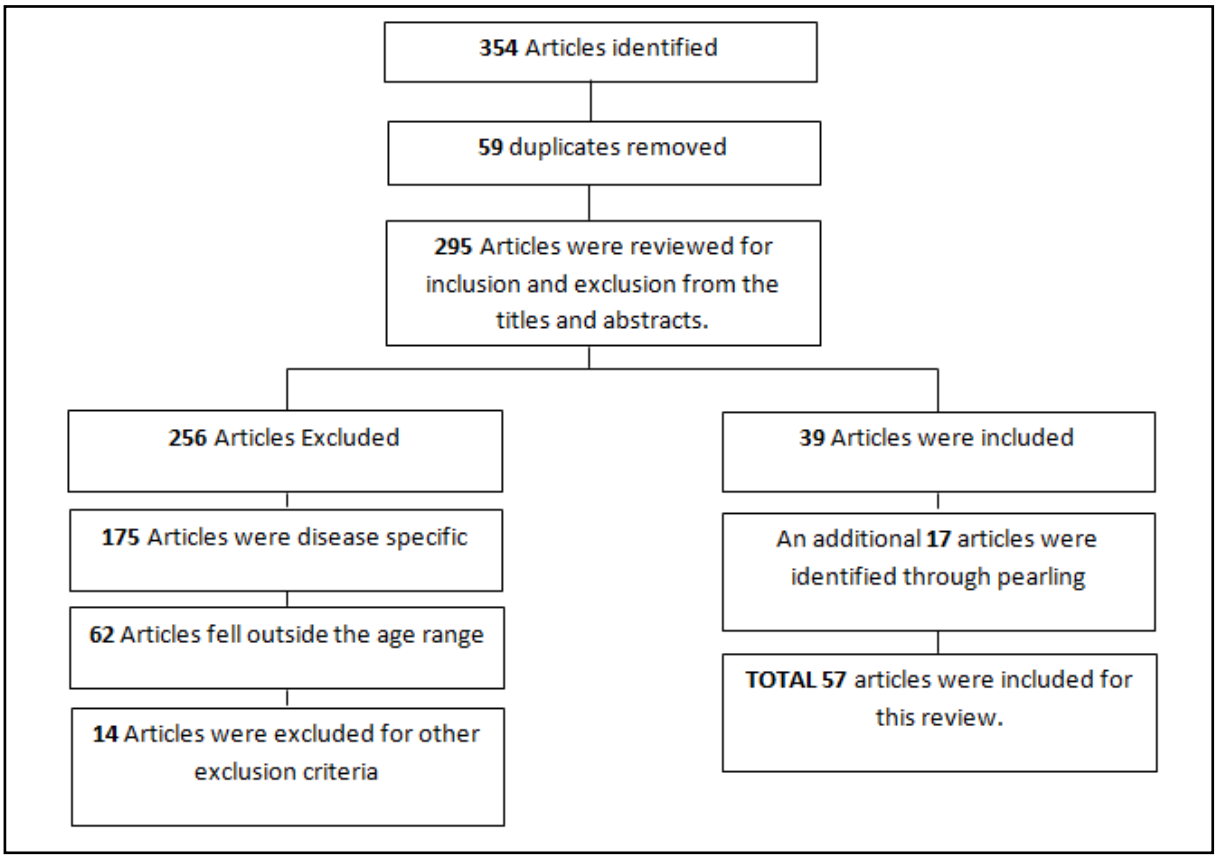


Figure 3-1: Search Outcome for Generic HRQoL Measures

3.3.2 Selecting a measure on which to model a new HRQoL Measure

3.3.2.1 HRQoL Instrument Development Procedure

3.3.2.1.1 Health Utilities Index (HUI)

The HUI is a product of more than 30 years of research, with theoretical and empirical evidence guiding the development of the HUI system [177], [178] (Appendix 1,Table 10-1). The Canadian system was designed to link directly with preference based scoring. The HUI: 1 was initially developed for CUA for very low birth weight infants in neonatal intensive care. The HUI: 1 made use of VAS and TTO methods to successfully develop utility scores. The development of the HUI:2 multi-attribute utility function was developed from the HUI:1 to assess the burden of childhood cancer but has since been applied to various groups [177], [178].

The HUI: 3 was developed from the HUI: 2 in order to better address the general population as well as clinical settings. Furthermore, the HUI: 3 was developed to demonstrate structural independence between attributes. They adapted the HUI:1 approach and utilised VAS and SG methods to develop utility scores [177], [178], [199]. The HUI: 3 should be used for primary analysis as it has a more in-depth descriptive system. The HUI:2 can be used to complement the HUI:3 data for secondary analysis for dimensions of self-care and emotion with regard to worry/anxiety and fertility [178].

3.3.2.1.2 The Health Status Classification for Pre-school Children (HSCS-PS)

The Health Status Classification for Pre-school Children (HSCS-PS) was derived from the HUI. The development of the measure was both Canadian and Australian (Appendix 1, Table 10-1). The dimensions were selected from a series of studies on the development and refinement of the HUI system. After the identification of the dimensions the existing levels were adapted based on age-appropriate developmental tasks. This was determined through examination of standardised tests, experts in the field and pilot exercises. The content of the measure was validated through a series of pilot exercises by developmental paediatricians and neonatologist. Field testing of the measure was conducted with the target respondents, clinicians and parents [174].

3.3.2.1.3 The Pediatric Quality of Life Inventory (PedsQL)

The PedsQL was derived from the PCQL which was a developed from the cancer database. The United States of America (USA) measure was designed as a generic measure from the WHO core health dimensions

to be used across the paediatric population (Appendix 1, Table 10-1). The PCQL item generation was based on extensive literature review, open-ended questionnaires with patients and their family and discussions with health-care providers. The development of the measure was in three phases each with a testing component until a satisfactory measure was developed [73], [200], [201]. The infant version was developed based on the same theoretical framework after the successful implementation of the core generic module. Review of the literature and consultation with health care professionals formed the groundwork of the development. Parent focus groups and parent cognitive interviews with children younger than one year of age were conducted. The measure was pre-tested and field tested before psychometric testing [201], [202]. The measure for children aged 1 -12 months has 13 additional items than the scale for children aged 2-4 years. The measure for children aged 13-24 months has 22 additional items than the measure for children aged 2-4 years.

3.3.2.1.4 The Warwick Child Health and Morbidity Profile (WCHMP)

The Warwick Child Health and Morbidity Profile (WCHMP) was developed in the UK as a parent report measure of their child or infant's reported health and morbidity (Appendix 1,Table 10-1). It was designed for use in both research and the clinical setting to describe both cross-sectional and longitudinal HRQoL. Open ended interviews were conducted with parents exploring their understanding of concepts firstly with first tier questions followed by second tier questions. In line with the data gathered the suggested dimensions were modified to improve comprehensibility and acceptability, for the final measure [203].

3.3.2.1.5 DISABKIDS Chronic Generic Module (DCGM)

The development of the DISABKIDS Chronic Generic Module (DCGM) was collaborated in a European multi-national study (Germany, Netherlands, UK, France, Greece, Sweden, and Austria) and the process commenced with a thorough literature review (Appendix 1, Table 10-1). Thereafter, focus groups were performed with children and their caregivers where statements were recorded for item generation. The generated statement-pool was rated and reviewed by an expert panel who agreed on a final pool of 100 items. The English items were then translated into five other European languages before pilot testing to determine the final items for inclusion in the measure [204], [205].

3.3.2.1.6 DISABKIDS Smiley Questionnaire

The DISABKIDS Smiley Questionnaire (DSQ) was developed as part of the DISABKIDS project and was developed from the DCGM (Appendix 1, Table 10-1). A review of the literature was conducted followed by focus groups with children and their parents in seven European countries. The focus groups were recorded, transcribed and analysed for the development of the 12-item scale. The response categories of smiley faces was researched and accepted which guided the layout of the questionnaire. Pilot testing of the questionnaire was conducted and based on the results items were reduced, with an option of a six item measure. The final questionnaire then underwent psychometric testing [206].

3.3.2.1.7 The TZO-AZL Pre-school Children Quality of Life (TAPQOL)

The TZO-AZL Pre-school Children Quality of Life (TAPQOL) is another European (Netherlands) developed HRQoL measure. The dimensions were developed with findings from literature reviews, discussions with HRQoL experts and discussions with parents of children aged 1-5 years (Appendix 1, Table 10-1). A preliminary version of the measure was created based on the literature and psychological and clinical experience of the researcher. The measure, including sub-dimensions, was pilot tested on a group of parents and adapted before psychometric testing [207], [208].

3.3.2.1.8 The Child Health Questionnaire (CHQ)

The Child Health Questionnaire (CHQ) was developed in the USA as a broad perspective health outcome measure for use in health care, research and clinical trials (Appendix 1, Table 10-1). The aim of development was to construct a practical, comprehensive measure of functional status and well-being with good discriminant validity across conditions and healthy children from 5-18 years of age. The definition of health was adopted from the WHO with the physical and psychosocial dimensions of health impacting on the child's social role. The development process commenced with a review of the literature and existing measures. This information together with the authors' previous measurement experience core concepts was identified. The initial CHQ measure was constructed and tested on parents and children over 5 years of age. The data collected from these studies informed the inclusion of items in future versions. Thereafter, varying lengths of the form were created including the parent forms with items of 50 (CHQPF50) and 28 (CHQPF28)[209].

3.3.2.1.9 The Infant Toddler Quality of Life Questionnaire (ITQoL)

The WHO definition of health was adopted in the development of the Infant Toddler Quality of Life Questionnaire (ITQoL). The ITQOL forms part of the CHQ family for general quality of life and was similarly developed in the USA. It uses both the WHO definition of health and developmental guidelines which are similar to the CHQ allowing for a continuous measurement of HRQoL (Appendix 1, Table 10-1). The ITQoL questionnaire has also been reviewed with a reduction of items allowing for either a 97 or 47 item measure [210], [211].

3.3.2.1.10 The Kiddy-KINDL^R

The Kiddy-KINDL^R forms part of the German developed KINDL^R package of measures (Appendix 1, Table 10-1). It was developed from the KINDL^R which was a conceptual model where children were interviewed on the four main components of QoL. Thus, it takes into account the progress of the child during typical development. Items were constructed from the accumulative data and pre-tested in two pilot studies. The KINDL^R was then included in a three year environmental, psychological observational study. The subsequent developmental process of the Kiddy KINDL^R is unclear from the literature [212].

3.3.2.1.11 The Quality of Life Measure for Children (C-QoL)

The Quality of Life Measure for Children (C-QoL) was developed to measure the difference in HRQoL between Thai children living in urban areas and children growing up on construction sites (Appendix 1, Table 10-1). The questionnaire was modelled from the WHOQOL system and its definition of HRQoL. Focus groups with children, from families working on Thai construction sites, participated to determine the suitability to children and the appropriate use of language. Based on the data collected from the focus groups facets were deleted or altered. The response scale was examined. A child- and carer-form were developed and tested for psychometric rigour [213], [214].

3.3.2.1.12 Patient Reported Outcome Measurement Information System Pediatric Global Health (PROMIS PGH-7)

Patient Reported Outcome Measurement Information System Pediatric Global Health (PROMIS PGH-7) was developed in the USA with cognisance of existing literature and perspectives of the target population (Appendix 1, Table 10-1). From expert input and literature review the first item pool was created. They conducted cognitive interviews with 21 children (aged 8-17) and 15 parents. The individual's concept of

global health, their experience of health and their understanding of global health were examined. Parents reviewed the PROMIS global health items. With input from professionals and consideration of developmentally appropriate items a second item pool was developed. The new items were tested via a web-based survey and it was found to be useful to assess global health of children from 5-17 years old [152]–[154], [215].

3.3.2.1.13 TEDQoL

TEDQoL was developed in the UK as a self-report measure for children aged 3-8 years (Appendix 1, Table 10-1). The content of the items was developed based on a review of the literature and experience with children. The scale was administered using a forced choice recognition task with two identical teddy bears. Children identified with the description of one teddy bear as well as identifying with a 'happiness' Likert-type scale of four faces. The first testing was then modified into TEDQoL (2) which asked only one question about the child's functioning and omitted the happiness question. The children were asked again to identify with the description of one of the teddy bears and then choose how much they were like the teddy bear on a Likert-type scale. The items were further grouped into five dimensions [216].

3.3.2.1.14 The Functional Status II(R) (FS II(R))

The Functional Status II(R) (FS II(R)) was developed in the USA in response to a need for a sensitive measure of functional ability for both ill and healthy children (Appendix 1, Table 10-1). For the purpose of the development of the measure child health was defined as the capacity to perform age appropriate roles and task. A thorough review of the literature formed the basis of the development procedure. Clinical experience and interviews with mothers informed the item pool generation. The behavioural responses to illness which interferes with normal performance of roles were used to define dimensions. The measure (FS I) was reviewed by a panel of experts for content, clarity and relevance to the construct to be measured. The form (FS I) was pretested before testing for psychometric properties. A revised version of the form FS II (R) was developed after results from the psychometric testing of FSI [217], [218].

3.3.2.1.15 EuroQol – 5 Dimension – Youth (EQ-5D-Y) Proxy Version

The EQ-5D-Y was based on the adult version, EQ-5D, to enable younger respondents to self-report (Appendix 1, Table 10-1). The intended applications include population health surveys, routine measurement and monitoring in health care settings and clinical research and practice [106], [219]. The

development process was guided by an international task team under EuroQol (Germany, Spain, The Netherlands, Sweden; Italy; UK; South-Africa) [144]. The first step in the process was the review of the EQ-5D dimension definitions by the expert committee to determine the pertinence to the target age group of 8-18 years of age. Particular attention was given to the appropriate developmental stages of both childhood and adolescents. Based on previous experience with administering the EQ-5D to younger respondents as well as previous results from qualitative assessments the EQ-5D wording was revised to optimize comprehension [144]. The provisional questionnaire was translated for cognitive interviews in four European countries. Healthy and chronically ill children and adolescents were included in the cognitive interviews with the aim of investigating comprehensibility, possible misinterpretation and acceptance of the questionnaire. The results informed the necessary changes before the questionnaire was tested for construct validity, including convergent and divergent validity [144], [145], [220], [221]. Thereafter the measure was re-worded for proxy evaluation and the age-range of the proxy version was extended from 4 – 18 years of age. The proxy version was translated and tested in Spain [40], [222].

3.3.2.2 Observability of Dimensions and Consideration for Inclusion in a Future Item Bank

The dimensions of health that are included in a measure should demonstrate the perspective of the target population [15], [141]. However, the inclusion of dimensions was most often initially based on expert opinion which were changed or excluded according to results from focus groups or pilot testing. The WHO's definition of health and the components of HRQoL namely physical; emotional, social and cognitive dimensions are most often used as a theoretical basis in the development of the measures.

As seen in Table 3-1 the number of dimensions included in the measures ranged from 3 – 13. Based on the names of the dimensions all measures had a dimension that encompassed or included physical function. The emotional or behavioural aspect of HRQoL was included in all measures but the C-QoL and FS II (R). Social functioning or relationships were included in all but three measures (HSCS-PS; WCHMP; FS II (R)). Cognition or school functioning is included in five of the measures (HSCS-PS; PedsQL; TAPQoL; HUI; TEDQoL). Pain is categorised separately in six of the measures (HSCS-PS; HUI; CHQ; ITQoL; PROMIS PGH-7; EQ-5D-Y). Self-care is included in six of the measures (HSCS-PS; HUI; Kiddy-KINDL^{R}; C-QoL; FS II (R); EQ-5D-Y). General Health is prioritized in four of the measures (HSCS-PS; WCHMP; CHQ; ITQoL). Other dimensions included include the: sensory system; self-esteem; growth and development; family cohesion; environment; spirituality; personal beliefs; energy; sleeping; eating; toileting patterns and fatigue. Most of the questionnaires included dimensions as described by the WHO and the dimensions could be matched to the ICF concepts except that the environmental factors are very poorly represented. If the dimension of

fertility on the HUI is not appropriate (as with children) it is recommended that the dimension is not completed but full health (1) is scored for that dimension when calculating the utility score [223].

- HUI and HSCS-PS both define different levels with a long, ambiguous description for every item e.g. seeing "close to oneself" is at arm's length; seeing "at a distance" means across the street. "Small objects" means as small as a penny. However, they give a good objective observable description for all dimensions except for emotion and pain. The HSCS-PS further gives operational definitions for terms which may be difficult to understand in the description.
- The PedsQL has many items under each dimension. Most of the items which describe the physical functioning dimension are observable but a few are not. With the school/cognitive function dimension all of the questions are observable. The emotional and social functioning items are not based on observable dimension.
- The WCHMP has a good description of minor illnesses and accident status as well as a specific question on hospital admissions which is based on occurrence rather than observable behaviour. The other questions rely on a subjective rating according to the proxy.
- DCGM and DSQ proxy questions are posed from the viewpoint of the child and it thus makes objective observable questioning difficult. Thus, not one of the questions is asked in such a manner that they are assessing observable behaviours.
- The TAPQoL questions ask the parent to report on frequency of a physical system followed by the quality of how the child felt during that period. The first response set to the questions for the physical dimension is based on observed behaviour. The question that follows 'At those times, my child felt: well; not very well; unwell; very unwell' [207] is not necessarily observable as children may not verbalise how they are feeling accurately. Thus there may be both over- and under-reporting of problems from the child and/or from the proxy.
- In the Kiddy-KINDL^{R} every day functioning items are very well described with regards to observable behaviour. The rest of the questions are not described by observable behaviours.
- The CHQ does acknowledge the importance of observable dimensions as described by the FDA [33], [209]. However, not all of their items are based on observable function. Notably they did word the dimension of emotion and behaviour very well reflecting observed behaviour: 'During the past four weeks, has your child been limited in the AMOUNT of time he/ she could spend on schoolwork or activities with friends due to EMOTIONAL difficulties or problems with his/her BEHAVIOR?' [209]. For the other items under the behaviour dimension there is reference to the behaviour of other children which brings in an observable component.
- ITQoL is very difficult to comment on as there was no measure available to review the wording of the items. From the focused concepts described on the *healthactchq* website the physical activity is

described by the amount of limitation; which one would assume is observable. Pain is described in terms of frequency as well as the extent to which it interferes with normal activity – the observability can be debated. Behaviour and moods are both described by observable behaviours and rated on a scale of frequency. The parent satisfaction with development and perception of behaviour and health would be subjective [224].

- The PROMIS PGH-7 does not have any of its functions based on observable functions.
- The TEDQL is a self-report measure therefore analysis is not applicable.
- The FS II (R) has many observable dimensions of note: sleeping; eating; toilet patterns and general health. The unobservable items are similar to the other measures and include: communication; mood and energy.
- The EQ-5D-Y proxy version has five dimensions of which walking about, looking after one's self and usual activities are observable. As with many of the other measures the dimensions of pain and worried, sad or unhappy are not observable.

Table 3-1 Descriptive Dimensions Across Generic HRQoL Measures

Dimension	HUI	HSCS-PS	PedsQL	WCHMP	DCGM	DSQ	TAPQOL	Kiddy-KINDL^{R}	CHQ	ITQOL	C-Qol	PROMIS PGH-7	TEDQoL	FS II(R)	EQ-5D-Y
Physical	X	X	X	***X***	**X**	**X**	X	X	X	X	X	x	X	X	X
Social			***X***		**X**	**X**	***X***	***X***	***X***	X	X	X	X		X
Cognitive	X	X	X		**X**	**X**	X	X	***X***				X		
Emotion	***X***	***X***	***X***				***X***	***X***	X	X		X			***X***
Self-Care	X	X		***X***				X	X		X			X	X
Pain	***X***	***X***							***X***	X		X			***X***
Behaviour		X		***X***						X				***X***	
Self-esteem								***X***	***X***		X		X		
General Health		X		***X***						X				X	
Dexterity	X	X													
Time									X						
Environment											X				
Religion											X				
Communication														X	
Child's Rights											X				

**Bold and italicised dimensions are not based on observable behaviour.*

3.3.2.3 Items

All the measures make use of a Likert-type scale, ranging between three and six response options, except for the TEDQoL (Appendix 1, Table 10-1). The TEDQoL makes use of a dichotomous scale for ascertaining which teddy bear the child best relates with a Likert-type-type scale measuring the relativity of the relationship. A Likert-type frequency scale (never, sometimes, often) is used in four of the measures (PedsQL; Kiddy-KINDL^{R}; DCGM; DSQ). A Likert-type quality scale (excellent, average, poor) is used in three of the measures (HUI; HSCS-PS; PROMIS PGH-7). Four of the measures make use of mixed Likert-type scales depending on the question (WCHMP; TAPQoL; C-QoL; CHQ; FS II (R)) and a frequency scale together with quality (CHQ; TAPQoL; WCHMP) and likelihood (always; usually; often; sometimes; never) (CHQ; FS II(R)). The EQ-5D-Y is the only measure to make use of a quantity scale (no problems, some problem and a lot of problems). The DSQ makes use of pictorial response options with smiley faces. The C-Qol makes use of

'finger pictures' for intensity, capacity and importance scales, smiley faces for evaluation scales and clocks for frequency scales. The WCHMP has both Likert and open ended questions.

The number of items range from 5 – 97 items per instrument (Appendix 1, Table 10-1). Many of the measures have the option of completing either a full or shortened version of the scale. All but four of the scales have an option of less than 25 questions (TAPQoL; CHQ; ITQoL-QoL). The PedsQL infant scales have a high number of items with 36 and 45 items for the 1-12 month and 13-24 month age groups respectively.

The HUI questions make reference to how the child carries out the function in comparison to children of a similar age. This is seen in some of the questions in the WCHMP; CHQ and ITQoL but the majority of the questions in these measures are referenced to the child themselves (PedsQL; TAPQoL; DCGM; DSQ; C-QoL; PROMIS PGH-7; TEDQoL; Kiddy-KINDL^{R}; FS II (R); EQ-5D-Y) (Appendix 1,Table 10-1).

3.3.2.4 Recall Period

Many of the measures do not specify a recall period (Appendix 1, Table 10-1). The PedsQL specified for the last (one) month, the TAPQoL was three months and the PROMIS PGH-7 specified seven days. The HUI had options of asking either current; past week; past two weeks or past three weeks. The CHQ had a four week recall period except for three of the questions. Similarly, the ITQoL also ranged from current to past and future for different questions. The DCGM specified four weeks and the FS II(R) specified the last two weeks. The WCHMP specified a recall time of one year in three of the ten questions. The EQ-5D-Y has a recall period of today.

3.3.2.5 Summary Score and Preference Based

- A psychosocial health score; physical health score and a total score can be calculated for the PedsQL [201]. If more than 50% of the items are missing the scores should not be calculated. There is no weighting of items for the measure. The scoring procedure commences with reversing item scores on a linear scale from 0-100. The mean dimension scores are simply calculated by adding the score of the items and dividing it by the number of items answered for that dimension [201]. Thus the psychosocial health summary score will be calculated using the items from the emotional, social and school functioning scales. Physical health summary score is just the score from the corresponding dimension and the total score is calculated with all of the items on the measure. A higher score indicated a better HRQoL [201]. Normative data could be collected as a reference for researchers, this has however not been done to date.

- DCGM consists of six sub-scales which can be combined to represent the three dimensions of HRQoL: mental (independence and emotion); social (inclusion and exclusion) and physical (limitations and medication). The dimension scores can further be combined to give a total HRQoL summary score [225].
- DSQ gives a single summary score with the addition of the six or twelve items. This score can be compared to scores on a reference table which was developed using the scores from children in seven different countries [225].
- The TAPQOL was shown to be a true HRQoL scale which showed multi-dimensional constructs as the correlation between dimensions on the measure was low. For each set of items under a dimension a separate principal component analysis was performed which resulted in only one factor being extracted indicating uni-dimensionality. All of the items, except two, had a higher item-rest correlation with their own dimension than other dimensions. This all supports the scale structure [207]. Thus, dimension scores are added and transformed to a scale of 0-100 with a higher score indicating a better HRQoL [208].
- The CHQ went through a comprehensive process for obtaining their scoring algorithm. In the study to measure the internal consistency of the measure five out of the eight scales exceeded 0.74, in a total normative sample. Internal consistency methods have shown that the Physical Health Summary Score (PhS) and Psychosocial Summary Score (PsS) measures are reliable [209]. The PhS and PsS are linear combinations of ten scale items measuring distinct constructs. Internal consistency reliability of each scale has been proven. The scoring process for the CHQ is done using computer software and can be summarised as follows. Raw scores are calculated for the CHQ by computing the algebraic mean of the items. One needs to transform the raw scores from 0-100 with a higher score indicative of better health. Thereafter scoring of the PhS and PsS is done according to weighted scores. During the testing for the scoring algorithm 10^2 CHQ measures were standardized using means and standard deviation for the general US Population. The scales were further assigned weights using factor score co-efficient. The PhS and PsS are standardized using a T-score transformation. The advantage is that results can be meaningfully compared with other scores obtained from the general population. Due to the fact that the standard deviation is 10 for both PhS and PsS each one-point difference has a direct interpretation[209].
- There is no indication in the published literature on the website that the ITQOL has any form of scoring.
- The Kiddy KINDL^R developed its scoring structure using item analysis and reliability analysis using the Multi-Analysis Program (MAP). This programme utilises Campbell's multi-trait approach and performs confirmatory analysis of the hypothesized scale structure. Furthermore, it shows between the individual items and the overall scale [212]. This was shown on a German study with

chronically-ill children, adolescents and parents with a consistency co-efficient α>0.8 and Cronbach's alpha α=0.70. Sub-scale and total scores represent a quantification of the child's HRQoL from the proxy's point of view. The values can be assessed by the distance from minimum (0) and maximum (100) scores for an indication of the child's functioning within a dimension or overall HRQoL. One can compare the scores with population scores according to age-group and sex. The scores from the standard sample is based on the results from a large sample of German school children (n=1501). One can further monitor the change in a patient's clinical condition due to a change in that individual's dimension and total score. Scores can be calculated with a computerised analysis program (available free of charge) which both reverses the item scores and gives dimension scores and a total score. Subscale scores cannot be calculated if there is more than 30% data missing. A higher score implies a better HRQoL [212].

- The PROMIS measures were all prepared for scoring in a study in the US general population. Data was collected from 21 133 members of the general population and disease population to: create item calibration for each dimension; estimate profile scores for various disease populations; creating linking metrics to legacy questionnaires (e.g. SF-36); confirm the factor structure of dimensions and conduct item bank analysis [226]. There is normative data which is age-adjusted (adjusting for developmental changes); fully-adjusted (adjusted for demographic details) and unadjusted (for comparison to the general population) [227]. In order to score the PROMIS PGH-7 the respondent must complete all of the items. The scores require re-coding so that the higher score indicates higher functioning. The raw scores are simply added together and converted to a T-score using the T-Score Conversion Table. These T-Scores can also be used to link metrics to a legacy questionnaires [226], [227].
- The EQ-5D-Y does not have a summary score or utility index currently. Research is however, underway to value the EQ-5D-Y measure [39].
- The HUI is the only preference based measure and can be applied to both clinical and general populations for people five years and older. The HUI used a multi-attribute approach in deriving their scoring: the utility scores from a sample of the general population and the HRQoL score were derived using a 100 point VAS with the SG chance board to assess a series of health states [178].

3.3.2.6 Practicality

Practicality can be assessed in several ways including: ease of completion, response rate and administration (Appendix 1, Table 10-2).

- Completion time was measured for eight of the measures; with time ranging from 1 – 15 minutes with the exception of the C-Qol which was reported at 30 minutes (HUI; HSCS-PS; PedsQL; WCHMP; DSQ; Kiddy-KINDL^{R}; C-QoL; PROMIS PGH-7) (Appendix 1, Table 10-2).
- Response Rate was measured for of the two of the measures and ranged from 67 -95% (TAPQoL; ITQoL). The percentage of missing values was recorded in the testing of five of the measures and ranged from no missing data to 15.4% (HUI; PedsQL; DCGM; TAPQoL; ITQoL) (Appendix 1, Table 10-2).
- The Literacy level was commented upon in five of the measures. The HSCS-PS is reported as having a literacy level of Grade 8. The CHQ and the PedsQL measuring between Grades 3.2 -3.5 and Grades 1-3 respectively on the Flesch-Kincaid readability score. The DSQ was found to have child-friendly wording and pictures. The EQ-5D-Y was reported as having excellent comprehensibility with low perceived difficulty scores (Appendix 1, Table 10-2).

In LMIC, such as South Africa, the cost of the instrument is important as we would like to encourage the use of routine outcome measurement in clinical practice and an increased research output without cost being a negating factor. With regard to the cost of the instrument (Appendix 1, Table 10-2):

- The HUI is available at an approximate cost of $5000 for use of one questionnaire version and the manual which applies to all users. From the registration on the website a request to register for a copy of the manual and questionnaire was denied as this was a review paper only [228].
- The HSCS-PS and the WCHMP are both free of charge and permission needs to be obtained from respective authors.
- The PedsQL is free of charge to individuals wishing to carry out non-funded academic research. There is a cost of $990 for one module for funded academic research and a larger fee for commercial use [181].
- DCGM and DSQ are both available at a cost of €60 (at time of going to press) for non-funded academic research for the manual and use of the questionnaire is free. For commercial and large non-commercial studies a fee will be calculated according to the sample size [225].
- The CHQ and ITQoL are both subject to a license agreement and the fees are calculated based on: the type of research project; funding source; patient/family sample size; number of completions of the measure by participants; number of study sites; study start and end dates; survey language.

Unfortunately a license agreement was not reached for the means of this research as it is a mapping review [224].

- The Kiddy-KINDL^R and EQ-5D-Y are both free of charge for researchers with a fee for commercial use [229].
- The C-QoL and the TEDQoL are not available on the internet but copies of both are available in the respective articles [34], [213].
- The PROMIS PGH7 is free of charge.
- The FS II(R) requires agreement from the author and a $25 dollar fee, (this information was updated in 2004)[230].

3.3.2.7 Psychometric Properties

3.3.2.7.1 Validity

- The face validity, which is poorly described in most of the publications, was mostly established through pilot testing of the measure with necessary adaptations before psychometric testing (Appendix 1, Table 10-2).
- The content validity was gauged from the development process of each instrument (Appendix 1, Table 10-2). Most studies reported that their measures were based on review of the literature and expert knowledge. Many of the measures conducted interviews or had focus groups with parents or children (PedsQL; WCHMP; DCGM and smiley; Kiddy-KINDL^R; PROMIS PG-7; FSII(R); EQ-5D-Y). Eight of the measures were developed from existing HRQoL measures (HSCS-PS; PedsQL 4.0; DSQ; Kiddy-KINDL^R; CHQ; ITQoL; C-QoL; EQ-5D-Y).
- Criterion validity was tested in 13 of the measures (HSCS-PS; PedsQL 4.0;WCHMP; DCGM;DSQ; TAPQoL; CHQ; ITQoL; Kiddy-KINDL^R TEDQoL; PROMIS PGH-7 PCH-7; FS II (R); EQ-5D-Y) (Appendix 1,Table 10-2). Measures were mostly correlated with scores obtained from a 'gold standard' HRQoL measure (FSII (R); Kiddy-KINDL^R; PedsQL; VSP-A; SF-36; TAPQoL) or other developmentally appropriate measure of function or health (Bayley Scales of Infant Development; Vinelands Adaptive Behaviour Scales, Bartlett's test of sphericity; Gross Motor Function Classification System; Health Records; Child Health Questionnaire; General Health Profile)
- The construct validity was tested in 13 of the measures (HUI; HSCS-PS; WCHMP; DCGM; DSQ; TAPQoL; Kiddy-KINDL^R; ITQoL; CHQ; C-QoL; PROMIS PGH-7; FS II (R); EQ-5D-Y) (Appendix 1,Table 10-2). Most of the associations were drawn between known groups of children (healthy; acutely-ill or chronically-ill children); between known medical conditions; or between parent and child or parent and health professional. Data reported for the EQ-5D-Y proxy was reported from the abstracts of two Spanish

studies and the details are thus lacking. All data reported for DCGM and Kiddy-KINDL^{R} was with participants over eight years of age.

3.3.2.7.2 Reliability

Internal consistency was reported for all but two of the measures (HSCS-PS; DCGM). The Kiddy-KINDL^{R} reported results were for a higher target age group than the age range stated for use. All studies had documented Internal consistencies which were moderate to excellent with $\alpha \geq 0.70$ (Appendix 1, Table 10-2).

Inter-rater reliability, between two different proxy respondents, was reported as good to moderate for three measures (HSCS-PS; WCHMP; HUI). Test-retest reliability was reported for seven measures and had good to moderate scores (HSCS-PS, WCHMP; DCGM; DSQ; ITQoL; PROMIS PGH-7; EQ-5D-Y) (Appendix 1,Table 10-2).

3.3.3 Selecting an Age Group for the New Measure

The PedsQL and FS II(R) both have different scales available for different age ranges respectively: 1-12months and 0-9months; 13-24 months and 10-24 months; 2-4 years and 2-5 years; 5-7 years and 6-11years.The Kiddy-KINDL^{R} also has two different versions for children aged 3-6 years and 4-6 years of age and can most likely attribute to the latter being a more appropriate age for self-report. There are three measures that assess the first five years of life on one scale WCHMP (0-5 years); TAPQoL (1-5 years) and ITQoL (2 months to 5 years). The HSCS-PS (2.5 – 5 years) and the TEDQoL (3-8 years) both begin assessment at a similar developmental period but the TEDQoL has a wider assessment period. The age range that is best represented is that from five years and onwards which may be attributed to the start of more formalised schooling and more clearly defined developmental progress HUI (5-8 years); DCGM and DSQ (4-7 years); C-QoL (5-8 years); PROMIS PGH-7 (5-17years) and EQ-5D-Y (4-17 years).

Proxy and/or Self- Report

The mode of completion of the measures was directly related to the age range for completion. All of the generic measures, except one (TEDQoL), included a proxy report measure, to be completed by the carer (Appendix 1, Table 10-1). The questionnaires that include children in the older age range generally had an optional self-completion questionnaire. The TEDQoL is the only measure that was developed for self-completion for children aged 3-8 years. The children are interviewed using two teddy bears each presenting a question and they are asked to choose which bear they identify with. All of the measures consider the view point of the proxy for completion except for the DCGM and DSQ which consider the view point of the

child. The EQ-5D-Y has two proxy versions to choose from: one from the view point of the child and the other from the proxy view point, the current recommendation is however, to use the version from the proxy view point [39]. Although studies have been done comparing the results from different proxy respondents such as mothers and fathers or parents and medical personnel [27] other factors such as the age of the proxy respondent or reliability of report from extended family does not seem to have been measured.

3.4 Summary and Discussion

The results of the review are summarised in this section and the implications of the findings is discussed regarding the objectives and *a priori* as described in the methodology.

3.4.1 Selecting a Measure on which to Model a New HRQoL Measure

3.4.1.1 HRQoL Instrument Development Procedure

The development procedure for most of the measures was based on the existing literature and the opinion of experts in the field of child development and HRQoL. The theoretical construct which was utilised was only referenced for a few of the measures (CHQ; ITQoL; C-QoL; EQ-5D-Y). Items included in measures that were derived from existing HRQoL systems were less representative of the developmental changes that occur in the age group. This is due to the fact that in most of the cases existing dimensions were adapted from existing measures to be more developmentally appropriate, rather than created to be appropriate. However, the PedsQL made particular note of that in the development of their infant scales with additional items representative of the milestones for the period. All of the measures showed evidence that they consulted parents or children in their development except for the HUI, HSCS-PS, TAPQoL and the ITQoL. Most of the measures conducted interviews or focus groups with parents of children. This is a valuable exercise and if done with parents of children in the age range for the measure important developmental changes can be reflected in the instrument. All of the instrument developers made reference to the fact that their developmental process considered age-appropriateness.

Pilot testing took place in most of the measures and changes were made according to the findings. All of the measures were originally developed for use in high-income, western countries, apart from the C-QoL and the EQ-5D-Y. The C-QoL was developed for use in Thailand to measure the HRQoL of children of Thai construction workers and South Africans participated in the development process of the EQ-5D-Y. Most of the measures have been validated in diverse cultures and with many language options after the initial

development. The EQ-5D-Y was the only instrument that took a cross-cultural approach during the development of the instrument. The dimensions and items for inclusion for most of the measures were, however, based on research and opinions from experts and parents or children from countries which are well resourced and have well established health and social services.

3.4.1.2 Dimensions Included in HRQoL Instruments

The dimensions were determined during the development stages mostly from the literature and from expert opinion. Parents were most often invited to comment on an item bank of possible dimensions which subsequently guided inclusion of items and dimensions. Most of the measures have multiple items describing each respective dimension (HUI; PedsQL; DCGM; DSQ; TAPQoL; CHQ; ITQoL; Kiddy-KINDL^{R}; C-QoL; TEDQoL; FS II(R)). Dimension inclusion was quite similar across measures with 15 measures including mobility/function, social dimension, cognition/learning, emotion and self-care included in eight measures. These dimensions were also generally the most observable dimensions on the measures. This was in keeping with WHO's definition of health and components of the HRQoL namely: physical; emotional; social and cognitive [47], [71]. The less observable dimensions of pain, behaviour, self-esteem and general health were not as well represented. Due to the similarity in dimensions reported across measures all of the dimensions from Table 1 will be included in an item bank for further testing. This item bank will be tested expanded and tested further in both cognitive interviews and expert opinion.

The observable characteristics of the dimensions were poorly defined in the literature. There is no measure that was based solely on observable behaviour. The DCGM, DSQ, WCHMP and PROMIS PGH-7 did not include any observability in their dimensions. The HSCS-PS, FS IIR, HUI and EQ-5D-Y had the highest number of observable dimensions. The PedsQL, TAPQoL, Kiddy-KINDL^{R} and CHQ all showed observability in at least half of their dimensions. Inclusion of observable dimensions would result in more accurate proxy report of HRQoL as it has been shown that observable dimensions such as physical activity correspond better between proxy and self-report than subjective outcomes such as emotion [35], [221], [231].

The issue of observability in a dimensions in children under five years of age has been recommended by both ISPOR [13] and the FDA [33]. These recommendations have been made in order to minimise subjectivity of the proxy reporter when completing proxy evaluation for very young children [13], [33]. This would in turn further improve the intra-rater reliability between two different proxy respondents.

There were no published consensus guidelines on the representation of certain behaviours within a dimension. In general within a dimension there were some observable and some unobservable items. The

measures would typically word the item in such a way that directly related to the dimension 'problem feeling afraid or scared'. However, sometimes the question would be very specific with regard to being included in play or forgetting things. In other questions there was ambiguity as three constructs were asked in one item 'feeling worried, sad or unhappy'. Ambulation and physical health seem to be the easiest dimension to measure with observable behaviour. If the age range covered by the measure was small enough gross motor milestones could be described more easily. Cognition was also seemingly more easily measured by observable behaviour as reference was most often made to pre-school specific tasks or ability to perform tasks of higher mental function. The dimensions of social, emotional and pain were generally poorly described by observable behaviour. Operational definitions, as developed from cognitive interviews; focus groups and review of the literature, could assist with ascribing behaviours to dimensions. As described in a pain scale incessant crying, inability to console, grimacing and change in tone could all be ascribed to pain in the non-verbal child [232], [233].

3.4.1.3 Items

The Likert-type scale was incorporated into every measure typically with three to five levels of response. A Likert-type scale with more than five levels of report or a questionnaire with mixed methods could be considered a higher cognitive burden on the respondent [143]. The Likert-type frequency scale (never, sometimes, often) was most commonly implemented, in four measures, followed by a quality scale, in three measures (excellent, average, poor). Additionally four of the measures used different Likert-type scales depending on the dimension or item measured. The DSQ made use of smiley representation together with wording. Likewise the C-Qol made use of 'finger pictures' for intensity, capacity and importance scales; smiley faces for evaluation scales and clocks for frequency scales. This assists younger children with assisted or self-completion.

The number of items on most of the measures had been reduced, allowing for two options for completion. The number of items and corresponding increase in completion time influences the acceptability and practicality of the measure in terms of burden of completion; missing values and drop-out or non-compliance with research. The cost of administering the measure is higher for measures with a higher number of items. The average number of items should be no more than 15 items if one considers the measures reviewed. However, if one is considering using the measure for health economic evaluations the greater the number of potential health states the more costly the development process. The measure should consider both the number of items and the number of response options for the item, for cost calculations.

The EQ-5D-Y and the PROMIS PGH-7 had the least number of items. The HSCS-PS, DCGM, DSQ and FSIIR all had versions with 15 or less items. The PedsQL had less than 15 items on their scales for children older than two years but not for the younger age groups. Similarly the Kiddy-KINDL had less than 15 items on their measure for older children for self-complete but a considerably higher number (47) on their proxy version for younger children aged 3-6 years.

3.4.1.4 Recall Period

The ITQoL and WCHMP had different recall periods for different items included in the measure. The HUI had different recall options which would apply to all items on the measure (current; past; one/two/three weeks) – this could make comparison between research groups or in clinical setting more challenging. The period of recall for the TAPQoL is three months which is an unrealistic time period for children in the age range of 1-5 years old due to the rapid developmental changes during this time. A month as specified for recall in the PedsQL; DCGM and CHQ could also be argued as a substantial period of time to recall behaviours or changes in a child. The FS II(R) and PROMIS PGH-7 gave a shorter reference period of two weeks and one week respectively. The EQ-5D-Y had the simplest recall period of today which substantially reduces the potential for recall bias [79]. The longer the recall period the more one is dependent on memory and the higher the potential that there is subjective or circumstantial overflow in the assessment of the child's HRQoL [79].

3.4.1.5 Scoring and Association with a Preference Based Measure

The majority of measures for children under the age of seven were generic health profiles and had either dimension scoring and or a single summary score. The process behind the scoring algorithms for the measures was generally very poorly defined in the literature. The measures generally had computer software or a tabular reference used to calculate dimension and/or summary scores. The process used to outline the analytical process was generally very briefly outlined to the user. Many of the measures simply add the scores together with no transformation of the ordinal scale to a cardinal scale. The CHQ gives a very comprehensive scoring process including individual weights allocated to items for both the PhS and PsS score. Scores obtained could also be compared to scores obtained from the general US population which has many advantages. The Kiddy KINDL^{R} scoring structure was developed using the MAP. The scores for both the sub-scales and the total score could be compared to scores obtained from a general German population. The PROMIS PGH-7 had the advantage of having US general population data for comparison on an age-adjusted, fully-adjusted or un-adjusted level. The scores could also be linked to legacy questionnaires for utility scores

The HUI was the only preference based measure with the generation of the utility index from the adult general population with both the VAS and SG. The utility score is indicated by death (0) and full health (1). This however not been extended to the HSCS-PS. The EQ-5D-Y is currently under consideration for assigning values.

3.4.1.6 Practicality

The practicality and feasibility of use of a measure was related to completion time and cost of the instrument. The completion times commented on were generally less than 10 minutes with the PROMIS PGH-7 being the most efficient with 1-2 minute completion time. The Kiddy KINDL^{R} took up to 15 minutes to complete and the C-QoL had a completion time of 30 minutes. Interestingly, the measure with the highest number of items, TAPQoL, completion time was not suggested. The HUI had a substantial $5000 fee attached to it. The CHQ and the ITQoL fees were not specified but were calculated according to the study design of the proposed research. A minimal fee was requested for the manuals of the DCGM and DSQ (€60), TAPQoL (€32) and the FS II(R) ($32). The other measures were free of charge. This was considered to be an important consideration for the practicality of the measure, especially in LIC and LMIC.

3.4.1.7 Psychometric Properties

The criterion validity of most of the measures was established through comparison to a previously developed and validated HRQoL measure. A high level of evidence was considered if these measures reported a high correlation. The divergent validity was most commonly reported on with confirming differences between known-groups. Content validity was judged from the developmental process of the measure. Face validity was reported from the results of the pilot or field testing during the development process. The internal consistency was reported as with an acceptable standard of $\alpha \geq 0.70$ for group comparisons and $\alpha \geq 0.90$ for individual comparisons for the PedsQL; DSQ; TAPQoL; CHQ; ITQoL; C-QoL; PROMIS PGH-7; FS II(R). The Kiddy-KINDL^{R} did not achieve $\alpha \geq 0.70$ for all scales. Similarly, the TAPQoL and WCHMP internal consistency ranged from 0.66 -0.90 and 0.55 -0.86 respectively. The TEDQoL scored less than satisfactorily at $\alpha = 0.60$. Test-retest reliability was generally very poorly reported on in the articles included for review. It is important to note that the psychometric data reported for the Kiddy-KINDL^{R} was calculated using a sample of children over the age of eight years. The EQ-5D-Y proxy form is reported on in two Spanish studies for which only the abstracts were available in English.

3.4.1.8 Selecting an Age Range for a New Measure

The age range of an instrument determines how accurately the developmental changes in the measure are represented. A wider age range was advantageous to the developers and researchers as a larger number of children could be compared with one measure but at the cost of the accuracy. Another consideration was that if the age range was large the proxy respondent would interpret the questions in accordance with the age of their child thus comparison between age ranges may be affected. It was considered as ideal if the age range for inclusion covered the spectrum with age specific versions but no study justified the specification of the age range for the respective measures such as was done with the PedsQL and the FS IIR. Many of the measures were more relevant of older children, typically from pre-school age; such was the HUI, HSCS-PS DCGM, DSQ, CHQ, Kiddy-KINDL^{R}, C-QoL, PROMIS PGH-7, TEDQoL and the EQ-5D-Y. The other measures included very young children but with a very large age span mostly from a few months to five years of age as with the WCHMP (0-5 years), TAPQoL (1-5 years) and the ITQoL (2 months – 5 years).

All of the measures had a proxy component except for the TEDQoL. The TEDQoL approached self-completion in this age group uniquely with children asked to choose the more relatable between two scenarios, represented by two teddy-bears. Proxy completion was favoured in this age group due to the cognitive ability of young children. Some of the scales had a self-report option for children at the higher limit of the age-group, typically over five years of age. Completing questionnaires from the view point of the child was only employed with the DCGM and DSQ measures. Although primary caregivers may have intimate knowledge of their young child due to close proximity, the child's limited communication may have influenced the extent of the shared knowledge [83]. The subjectivity of the respondent could also not be as well controlled with an association of emotional overflow from the caregiver being inevitable, especially in the case of illness [191], [192].

It is apparent that there is the greatest need for a measure for the youngest age group of children aged 0-3 years for proxy completion. The recommendation would be to model the instrument on a measure for older pre-school going children but following a rigorous development procedure to ensure content validity, observability of dimensions and applicability in South Africa. This would result in an instrument with a number of versions for proxy completion in young children as with the PedsQL and the FS IIR.

3.4.1.9 Summary of Selecting a Measure on which to Model a New Measure

Based on the above results the HSCS-PS, PedsQL; DSQ, PROMIS PGH-7 and EQ-5D-Y Proxy could be considered the most comprehensive generic HRQoL measures for children under the age of seven years. However, each was not without its limitations.

The HSCS-PS was derived from the HUI which was one of the oldest HRQoL measures and was embedded in years of research. As with all of the measures reviewed the HSCS-PS was lacking in a conceptual framework and justification of the age-range for inclusion. The development process was rigorous and took the target population and the opinion of experts in the field into account. The selection of the dimensions came from the HUI: 2 and HUI: 3 and similarly comprises of questions related to the senses. More than 80% of the items were considered to be based on observable. There were 12 items to complete but no reference period to time was given making it less valuable in longitudinal and cross-sectional studies. This further introduce bias in proxy reporting as it is not known for what period of time the proxy is considering. An advantage of the measure is that it is free of charge and easily accessible. Currently the HSCS-PS does not have any scoring system and can thus not be considered as a comparable preference based measure to the HUI. The psychometric properties of the HSCS-PS are sound. The measure was developed in Canada and Australia and shows good cross cultural validity across developed countries it has limited use in a LMIC setting with no cultural adaptation or validation studies done to date.

The development of the DSQ was rigorous and took into account the subjective nature of HRQoL measurement and addressed assisted report in children aged 4-7 years. There was further careful consideration given to the inclusion of smileys and layout of the questionnaire. Smiley faces may however, not be accepted and equivalent across all cultures [234]. One could choose from questionnaires with either six or twelve items. None of the dimensions were based on observable behaviours as recommended by both ISPOR and the FDA [13], [33]. The dimensions do not have a specified recall period which introduces further bias in the proxy completion of the measure and is s a disadvantageous for longitudinal and cross-sectional studies. The scoring system of the DSQ was lacking as there was no weighting of items and no transformation from ordinal to cardinal data. The score could however be compared to scores on a reference table developed using the scores from children in seven European countries. The psychometric properties of the measure are acceptable. Although much cross-cultural work has been done on the DSQ within European countries its transferability to LMIC such as South Africa has not yet been established.

The PROMIS PGH-7 is a newly developed HRQoL measure which belongs to a larger group of HRQoL measures. The development process of the measure was quite rigorous with a notable comprehensive

compilation of the paediatric item bank. It is a concise measure with seven items of report on a five level Likert-type scale with a relatively short recall period of 7 days. It had the advantage of being free of charge and quick to complete. None of the items were however, based on observable function. Although it had a comprehensive scoring system which could be linked to a legacy measure it was not a preference-based measure. The psychometric properties did not show entirely satisfactory results for item-scale correlation ranging from 0.30 -0.71. It was also implemented over a wide age range which allows room to question its developmental applicability. Furthermore, it is only applicable for the age range of 5-7 years for the population under review. Due to the relative age of the measure it has not yet shown wide cross cultural validity, most especially extending into LMIC such as South Africa.

The PedsQL is a comprehensive range of measures and has the advantage of having age specific measures. The developmental process of young children has been given much consideration with the specific scales for children aged 1-12 months; 13-24 months; 2-4 years and 5-7 years. The reference period of one month was quite substantial, most notably in the infant scales. The number of items is high, most marked were the 36 items on the infant scale. The dimensions were not based on observable function with some of the wording being particularly challenging 'feeling blue' and subjective. The scoring system of the PedsQL was a disadvantage as there was no weighting of items and no transformation from ordinal to cardinal data. Thus, statistical inference is greatly decreased and there can be no comparison to normative population data. The PedsQL set of questionnaires would currently be recommended for use in the very young age group as it was the most comprehensive with a wide range of items. It does however, not have potential to be used as a model for a new measure in very young children due to this wide age range. The dimensions from the PedsQL will be considered in the development of a new measure with the hope that the new measure will be better than the PedsQL with a firm basis on a conceptual framework, observable items and amenable to a scoring system which is beyond the scope of this thesis.

Although the EQ-5D-Y is a well-known and well-utilised measure as a self-report measure for children over the age of eight years, its utility as a proxy measure has not been explored, to date, in children younger than six years of age. This could be attributed to the fact that the EQ-5D-Y measure was only recently re-phrased for proxy completion. Furthermore, consideration of the developmental characteristics for the lower age range for completion (4-8 years) was not justified. Unfortunately, as with most of the measures extended for use, there is no appropriate measure for very young children. The measure has strengths in that it is short with five dimensions and has a simple recall period of today. It was one of the measures which included the highest number of observable items. The development process included cognitive interviews with children and collaboration with experts in the field. Furthermore, the development was carried out concurrently in seven countries including a LMIC, South Africa. It is also free of charge for

researchers. The current consideration for utility scores would add substantial value to the EuroQoL stable of instruments making effects of disease on HRQoL comparable across the lifespan. Although the validity and reliability of the proxy measure was only reported in two Spanish studies, it performed well in younger children, aged 6-18 years, in this population. The EQ-5D-Y may be considered the best model from which to develop a new measure for the very young age group. This would result in a number of instruments which would be able to measure HRQoL across the life span similarly to that of the PedsQL. The advantage of the EQ-5D-Y stable of instruments is that they are amenable to preference weights in the future.

3.5 Conclusion

There would appear to be a gap in the market for a generic, preference-based HRQoL measure for children under the age of seven years. But, most especially for the very young child under three years of age. Of the better performing measures only the PedsQL had versions appropriate for children in this age range. None of the above measures meet all of the *a priori*. If a new measure is to be developed, the EuroQoL model should be considered as an option on which to base the measure. This is due to the fact that the model is well-accepted internationally and the Youth version is culturally acceptable in South Africa due to its inclusion in the development process. Furthermore, the structure and parsimonious set of dimensions lends itself to valuation and it has the advantage of having a preference based weighting set available within the near future. There are however, further considerations which would need to be taken into account if it is to be used as a template for a new instrument. The development procedure should include focus groups or cognitive interviews with parents of young children and should not merely adapt the existing dimensions. The main aim of this process should be to identify dimensions and develop an operational definition of these dimensions based on observable behaviour.

The dimensions identified from the review of generic HRQoL measures should be considered for a future item bank. The age range of inclusion needs to be further defined together with parents and experts in the field. There may be a need to develop more than one measure to measure HRQoL in children under the age of three years and special attention needs to be given to the youngest and most vulnerable children. Due to the fact that the proxy version of the EQ-5D-Y has had limited testing in this age group, retesting in our context would be recommended. The measure should retain characteristics which define the EQ-5D-Y such as being short in length with well-defined levels of report and the recall period of today. If the measure is considered for a scoring system in the future there is a need to convert the ordinal data captured on the Likert scale to cardinal data using IRT at a minimum until a valuation exercise is undertaken to develop a value set.

It is recommended, based on the review that the development of a new HRQoL measure for young children should be considered, taking the above points into consideration, with special attention given to the very young age group.

4 Chapter 4: Cognitive Interviews with Caregivers of the Target Population

4.1 Introduction and Background

The results from the mapping review indicated that there was a need to develop a new HRQoL measure for very young children, particularly for children under three years of age. The EuroQol 3L model, i.e. five dimensions with three levels of report was identified as a suitable candidate to use as a reference point for the development of a new measure for several reasons. It is a simple instrument which has been widely used internationally with 4 986 published papers identified by a PubMed search of "EQ-5D". The Youth version of the instrument was developed multi-nationally with South Africa being one of the sites. Furthermore, the model is short in length, concise in the levels of report and has the advantage of an easy recall period of today. The proxy version of the EQ-5D-Y was unfortunately not widely tested and it was recommended that testing on the entire age group (0-7 years) be done simultaneously with cognitive interviews in order to determine and justify the developmental appropriateness and age range for inclusion. It may be further identified that a number of versions are needed for the age range between 0-7 years, as with the PedsQL. Thus a decision can be made for which age range, most likely between 0-3/4 years a new measure would be developed. In addition, a list of candidate items was identified during the literature review. Cognitive debriefing with caregivers of the target population would further inform the development of the item bank as well as the layout and wording for the new measure. The research questions for this study related both specifically to the EQ-5D-Y Proxy version but more generally they spoke to the content validity and layout. They included: Does the EQ-5D-Y perform well across all age groups? In other words, are the responses intuitively correct and is there known group validity? Do caregivers report that all the EQ-5D-Y dimensions are suitable for their children? Are there items that should be deleted and others added? How the questions should be framed with regard to the reference point (the child or their peers) and what reference point is used by the caregivers to respond to the different dimensions? Are the caregivers satisfied with the existing EQ-5D-Y layout template or have they suggestion as to how it can be improved?

4.2 Aim

The aim of the study was to explore the appropriateness of the EQ-5D-Y Proxy for younger children (0-7 years old) from the perspectives of the caregivers.

4.3 Objectives

The specific objectives were to determine:

- Whether the EQ-5D-Y proxy version displayed content validity across the age groups.
- Additional candidate items which could be added to the existing item bank, identified through the literature review.
- Which term of reference: norm (i.e. comparing the child's performance to other children of their age) or criterion (comparing the child's performance to their own 'normal' performance), was most often used by the caregivers in responding to the items.
- Whether the caregivers were satisfied with the existing EQ-5D-Y layout, and if not, what changes should be made.

4.3.1 Expected Outcomes

It was expected that the dimensions would be more relevant to children over the age of four years as this is the recommended age range for completion from the EuroQoL Foundation [39]. The dimension of looking after myself or self-care (SC) may not have been understood across all age-groups, most especially the 0-3 year group due to their dependence on this task ,and may have required age-appropriate descriptions [119], [235]. The descriptions provided under usual activities (UA) may not have been applicable to all ages and may have been better referenced against play [236] . Furthermore, the discrimination between the dimension of pain/discomfort (PD) and worried, sad or unhappy (WSU) may have been difficult, especially in the younger ages. The inclusion of two or three different concepts in one question was expected to be problematic as with findings from the mapping review (Chapter 3).

4.4 Methodology

A descriptive, cross-sectional study design with data collected by means of an interviewer administered questionnaire was carried out. This section of the research explored the thoughts and feelings of the caregivers with regard to their child's health, HRQoL and age. The questionnaire consisted of both closed ended and open-ended questions. The research settings included a tertiary level hospital managing both acutely-ill children and those suffering from chronic conditions and a day-care centre which accepted children of employees of the children's hospital from birth to seven years of age. The primary care-givers worked at the hospital and were accessible during working hours to participate in cognitive interviews.

4.4.1 Participants

The participants included caregivers of children aged from birth to seven years who were either acutely-ill (AI), chronically-ill (CI) or typically developing (TD). The inclusion of caregivers with children diagnosed with a spectrum of health classifications was important to ensure that the new measure and items was representative of the population for future use. AI children are categorized as those who were utilising the children's hospital in-patient facility and CI children as those who were utilising out-patient facilities at the children's hospital. TD children were categorized as attending an English day care centre.

Caregivers of children under seven years who accessed chronic health care services or acute health care services, 24 hours or later post admission were included. Caregivers of children under seven years who attended the day-care centre were included. The caregiver of the child were defined as any person over the age of 18, who lived with the child and was wholly or partly responsible for the care of the child's physical and emotional needs e.g. mother, father, aunt, uncle, grandparent, brother or sister.

Caregivers of children who were medically unstable, terminally ill or who were born prematurely and had not yet reached the corrected age of birth were excluded. An unstable child was classified as any child who was less than 24 hours post admission to ICU, less than 24 hours post-surgery or any child who had any acute changes in their medically condition within the past day.

4.4.2 Sample Size Determination

A non-probability, stratified sample of convenience from the in-patient, out-patient and day-care centre setting was used. The discriminant validity between TD, CI and AI children as tested by the Analysis of Variance (ANOVA) was used to determine the sample size based on the perceived rating of health (VAS). The calculation was based on a *root-mean-square standardised effect* (RMSSE) of 0.56 which was calculated based on a South African study using the EQ-5D-Y [221] using an expected difference in VAS of 10 between the groups, a standard deviation of 18 across the three groups, with a Type 1 Error Rate of 0.05 (Table 4-1). A minimum of 27 children per group were required to ensure a power of 95% for a one-way ANOVA.

Table 4-1 Sample Size Calculation Difference in VAS scores ANOVA, 1-Way Fixed Effects

Number of Groups	3
RMSSE	0.56
Non-centrality Parameter (Delta)	6.17
Type I Error Rate (Alpha)	0.05
Power Goal	0.95
Actual Power for Required N	0.96
Required Sample Size (N)	**27**

In order to determine whether this sample size was adequate if the dimension scores were considered a calculation based on effect size [237] was computed using G Power version 3.1. The sample size was powered to detect a difference in proportions across the two broader age bands (0-3 years and 4-7 years) and the three levels of each domain for each institution. The degrees of freedom were thus [3 ages bands -1] = [3 levels -1] =3. It was anticipated that the effect size of the age bands would be moderate (0.4). A sample of 69 children was required to ensure a power of 80% with a significance level of .05.

Thus the total sample size required would be 81. As the children were being divided into seven pre-determined age categories the number was increased to 84, a multiple of seven. There were 12 participants in each of the age categories e.g. four caregivers of children aged 1-2 attending a day-care; four caregivers of children aged 1-2 who were acutely-ill; and four caregivers of children aged 1-2 who were chronically-ill.

4.4.3 Instrumentation

EQ-5D-Y Proxy

An international task team under the EuroQol group developed a valid and reliable self-report version of the EQ-5D for children and adolescents (aged 8- 18 years) namely the EQ-5D-Y [144], [145], [238]–[240]. The content of the instrument was considered from a developmentally appropriate stand-point and the language and layout of the instrument was revised accordingly. This was translated into different languages and pilot-tested on a multi-national sample of young people, before final development of the new instrument. As in the adult version, the questionnaire comprises of five HRQoL constructs with age appropriate descriptions: Mobility (Mob) 'walking about', self-care (SC) 'looking after myself', usual activities (UA) 'doing usual activities', pain and discomfort (PD) 'having pain or discomfort', anxiety and depression 'feeling worried, sad or unhappy' (WSU) [144]. Each item as described has three levels of report;

'no problems', 'some problems' and 'a lot of problems'. It also has a modified version of the VAS which is a vertical, graduated scale from worst imagined health state (0) to best imagined health state (100) on which the subject rates their overall health status. [144], [145]. The English version of the EQ-5D-Y has been validated in a multi-national context including South Africa [145]. The English paper version of the EQ-5D-Y Proxy 1 (Appendix 4) is a direct adaptation of the EQ-5D-Y for proxy completion for children aged 4-8 years [39]. The EQ-5D-Y Proxy has been validated in a Spanish study only [40]. There are currently two versions available: proxy version one which asks the respondent to rate the child's HRQoL from their viewpoint and proxy version two which asks the respondent to rate the child's HRQoL from the child's viewpoint. The current recommendation is to use proxy version one [135]. The EQ-5D-Y proxy version one will be used in this study and will be referred to from this point as the EQ-5D-Y Proxy. The English EQ-5D-Y Proxy was used as a proto-type English instrument will be developed and validated before translation.

Interviewer-administered Self-designed Questionnaire

After the completion of the EQ-5D-Y Proxy caregivers participated in a cognitive debriefing session guided by an interviewer-administered, self-designed questionnaire (Appendix 5). The questionnaire comprised of both closed questions (e.g. "Did you compare your child to other children or to their own normal behaviour?") as well as open-ended questions (E.g. "What behaviour did the child show that let you to that decision?") which explored the reasoning behind the completion of the EQ-5D-Y Proxy. This is in line with other survey data collection questionnaires in which the variables which rely on narrative data, use "either a pre-coding or post-coding scheme is chosen depending on the type of variable. The pre-coding scheme is usually chosen when all possible answers are known, such as gender, marital status, etc. If the possible answers are not known (e.g. medication) then the post-coding scheme is chosen, and accordingly the data are collected in textual format" [241] . Participants were further asked to comment on the relevance of the dimension to their child and the use of wording and examples in the EQ-5D-Y Proxy. The face validity of the questionnaire was supported by two independent researchers.

The questionnaire was designed taking into account the verbal probing technique which asked the respondent specific questions. The questionnaire was constructed on an electronic mobile data collection platform, Magpi, which was used by the interviewer to guide the interview. The interviewer verbally asked each of the questions (some of which may have had a choice of two to three answers) and their answers to these questions were further 'probed' in order to identify the reasoning behind their response to the question [127]. Probing was done through the use of scripted probes as seen in the questionnaire (Appendix 5). This method was selected due to the advantage that the interviewer was prepared for the interview and had control of the interview and the respondent did not require any training [127]. The

verbal answers given by the respondents were manually recorded, by the interviewer, with the use of a tablet on the electronic Magpi system.

4.4.4 Procedure

Ethical approval was obtained from the University of Cape Town (UCT) Human Research Ethics Committee (HREC) (HREC/REF: 336/2014) (Appendix 2) and the children's hospital (Appendix 3). Permission to access the care-givers was granted by the day-care centre management.

There were seven age groups: Birth<1year (0-1 year); 1<2 years (1-2 years); 2<3 years (2-3 years); 3<4 years (3-4 years); 4<5 years (4-5 years); 5<6 years (5-6 years); 6<7 years (6-7 years). For ease of reference children will be categorised in the age range in years, depicted in parenthesis.

The first three consecutive caregivers in the general medical ward of the children's hospital were included. Participants were first recruited in the B1 and then B2 medical ward from the first cubicle to the last cubicle in numerical order in each of the wards. The subsequent wards were done in the same manner from the first to the fourth floor of the hospital. The caregiver's eligibility was determined using a grid to record their children's age to ensure that there were four participants from each condition group per age group. Informed consent (Appendix 6) was taken, 24 hours or later, post admission to the acute hospital.
Caregivers were asked to complete the paper version of the EQ-5D-Y Proxy (Appendix 4). Cognitive interviews took place with the use of a structured questionnaire (Appendix 5) in the private counselling room situated in each of the wards respectively. The answers given during the interview were recorded on a tablet using the Magpi data management system for further analysis.

The first three consecutive caregivers from each of the predetermined age categories, who attended the out-patient physiotherapy department, were approached and invited to participate in the study. The caregiver's eligibility was determined using a grid to record their children's age to ensure that there were four participants from each condition group per age group. After an explanation of the study was given informed consent (Appendix 6) was taken and caregivers were asked to complete the paper version of the EQ-5D-Y Proxy (Appendix 4). Cognitive interviews took place with the use of a structured questionnaire (Appendix 5) in one of the private consulting rooms.

Caregivers from the day-care centres were identified from a list supplied by the day-care centre which detailed the children's names, date of birth, responsible caregiver and the department in which they worked. A study grid was completed to record the number of participants and their child's corresponding

age group. On the recruitment days the caregivers who were on duty at work were approached given the details of the study and invited to participate in the study. Informed consent (Appendix 6) was taken and caregivers were asked to complete the paper version of the EQ-5D-Y Proxy (Appendix 4). Cognitive interviews took place with the use of a structured questionnaire (Appendix 5) at a pre-arranged time and place which was convenient to the caregiver. The answers given during the interview were recorded on a tablet using the Magpi data management system for further analysis.

To ensure reliability, and reduce measurement error the respondent first completed the EQ-5D-Y Proxy thereafter the primary researcher conducted a one-on-one interview. The primary researcher administered all interviews in order to ensure that observer error was reduced.

4.4.5 Data Management

The verbal answers given during the interviews were simultaneously transcribed onto a tablet, with use of Magpi data management system, by the interviewer. Both the tablet and Magpi data management system were password protected.

4.4.6 Data Analysis

Statistical Analysis was conducted using Statistica Version 13. Descriptive analysis was done to analyse the data. For the questions with two to three options quantitative data analysis was performed. Inferential statistics were used to determine if there were differences in responses between the AI, CI and TD children and across age categories. Due to the fact that there was a clear increase in the importance of the descriptive dimensions of Mob and SC for children over three years of age, analysis subsequently focussed on two larger age groups being those younger and older than three years of age. Frequency (ordinal data), median (ordinal and categorical data), range and mode (categorical data), were used to describe the data. The Shapiro-Wilk Test (numerical data from the VAS) and the Kolmogorov-Smirnov test (ordinal data) tested the normality of the data. Non-parametric tests (median and Spearman's rank correlation) were utilised for ordinal and non-normally distributed data. Parametric tests (mean, standard deviation and Pearson's correlation co-efficient) were utilised for normally distributed numerical data. The Chi-squared test was used to determine the goodness of fit of the dimension scores (categorical data) according to condition groups and age groups. To distinguish if there was any difference between VAS scores between AI, CI and TD children one-way ANOVA was used. Post Hoc Analysis was used to identify VAS means for AI, CI and TD children, which were different from each other. Regression Analysis of the VAS scores was used

to determine the effect that the dimension scores had on the VAS. The level of statistical significance was set at $p \leq 0.05$.

The responses to the open ended questions were post-coded and inductive coding, often called 'grounded' coding was utilised as the codes were generated from the data [242]. The primary researcher analysed the data for recurring themes, which were coded. A list of codes and a brief explanation thereof was subsequently drawn up by the primary researcher. The list of established codes was discussed by the two researchers to ensure comprehension. The agreed upon code list was then used by the second researcher who independently coded the data. The coding discrepancies were discussed until consensus was reached. In this way the narrative information was transformed into responses the frequency of which could be counted.

4.4.7 Ethical Considerations

Ethical principles of autonomy, confidentiality, beneficence/non-maleficence and justice applied in the cognitive interviews are detailed below and were based on the Helsinki Declaration [243]. The principle of autonomy ensures that the participants' in the study are provided with all of the necessary information so that they are able to pass their own judgements. This includes maintaining the participants' confidentiality and privacy throughout the study. Beneficence/non-maleficence ensures that engagements are to the participants'' benefit and that all potential harm is removed. Justice ensures that the burden or benefits of participating in the study is distributed equally among all potential participants'. This study was limited to English speaking participants.

Autonomy

Prior to commencement of the study, consent was obtained from the children's hospital where the study was to take place (Appendix 3). All participants who met the inclusion and exclusion criteria were given an information pack which detailed the purpose of the study, their role in the study, the risks and benefits, the confidentiality of their information and their right to refuse to partake in the study or withdraw at any point (Appendix 6). This information was further explained by the researcher, if any clarification was needed. Thereafter informed consent (Appendix 6) was obtained from each of the participants who had given consent of their own free will.

Confidentiality

The confidentiality of each participant was maintained by keeping the information in a secure locked cupboard and their names were deleted during the data analysis process. The electronic files were

password protected on a secure computer. No participants were identified in the analysis or write-up of the research.

Beneficence and Non-maleficence

The data collection did not affect the medical treatment which the child received or the way in which the caregivers were perceived at the health institution. The participants did not incur any costs for their involvement in the study and thus no monetary re-imbursement was given. The research had a potential to develop a new HRQoL measure, for very young children, which would be valid and reliable for use in children in South Africa. This would have had future benefit in measuring the HRQoL of very young children. This could have assisted in improved understanding of the child's health condition and could improve management thereof. If any developmental or maladaptive behaviour concern had been raised by a caregiver referral of the child to the relevant practitioner would have been made, with their consent. None of the participants raised any concerns about their child's development or behaviour which was not already being managed by a relevant health care practitioner. If any signs of neglect or abuse were noted referral to the necessary authority would have been made, in line with legal requirements. This scenario did not arise. There were no known risks to the participants and therefore no insurance was required for research-related injuries.

Justice

Every caregiver who was eligible to participate in the study was recruited. Caregivers across a range of socio-economic backgrounds were recruited and no-one who met the entrance criteria was excluded on the grounds of ethnic group, gender preference, religion or any other reason. Only caregivers seeking care for their children at the children's hospital or working at the children's hospital were eligible. This may have narrowed the social profile of participant's.

Due to the fact that a proto-type English version of the measure was being developed only English speaking caregivers were recruited. This limited the eligibility of a great number of the caregivers AI and CI children as the majority of caregivers utilising the hospital's service were Afrikaans or Xhosa speaking.

4.5 Results

Caregivers of 84 children were approached to complete cognitive interviews. Three groups of caregivers were included: 28 caregivers of AI children; 28 caregivers of CI children and 28 caregivers of TD children. No-one refused participation.

4.5.1 Descriptive Statistics

Of the caregivers who participated in the interview 74 were female and ten were male. Gender did not differ by condition groups and gender was independent of condition group (Chi-sq= 0.75, p=0.7). Mothers accounted for the highest number of caregivers (n=64) and fathers (n=9) were spread equally between the condition groups. The other caregivers included grandmothers (n=4), aunts (n=3), foster mothers (n=3) and a step father (n=1). The Chi-squared test indicated that the relationship of the caregiver to the child did not differ by condition groups and relationship of the caregiver to the child was independent of condition groups (Chi-sq=10, p=0.44).

Table 4-2: Education Levels of Caregivers Across Condition Groups

Education	**AI (n=28)**	**CI (n=28)**	**TD (n=28)**	**Totals (n=84)**
Primary and Secondary Schooling	14	17	8	39
Percentage	35.9%	43.6%	20.5%	
Tertiary Education	5	8	20	33
Percentage	15.2%	24.2%	60.6%	
All Groups	19	25	28	72

*Chi-sq=12.2, p=0.002 *Not all caregivers completed basic schooling*

The proportion of caregivers with a tertiary education was significantly higher in the caregivers of TD children (p=0.002, Chi-sq = 12.2) (Table 4-2). The children of the caregivers included 48 males and 36 females. Chi-squared results indicated that the gender of the child did not differ by condition and that gender was independent of condition (Chi-sq = 0.29, p=0.86).

There were 12 children in each of the six age group with four AI, four CI and four TD in the respective age group.

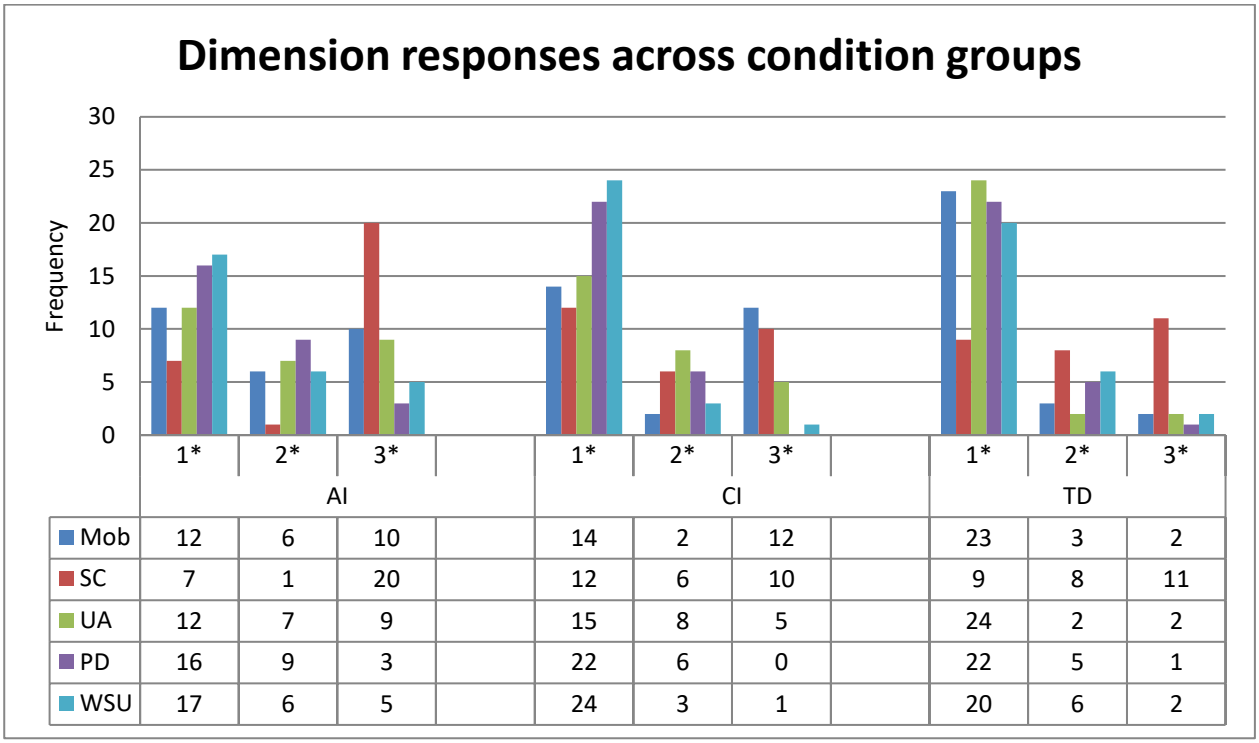
Table 4-3 Diagnosed Health Conditions of Children according to Condition Groups

	AI (n=28)	**CI (n=28)**	**TD (n=28)**	**Totals (n=84)**
None	0	0	**26 (92%)**	26(31%)
Cerebral Palsy	1 (4%)	**9(31%)**	0	10(12%)
Genetic	**5(18%)**	**5(18%)**	0	10(12%)
Respiratory Illness	3 (11%)	**6 (21%)**	0	10(12%)
Congenital Heart Defect	**6 (21%)**	3 (11%)	0	10(12%)
Neurology	**5(18%)**	3 (11%)	0	8(9%)
Surgery	4(14%)	1 (4%)	0	5(5%)
Pneumonia	2(7%)	0	0	2(2%)
Gastroenteritis	2(7%)	0	0	2(2%)
Failure to Thrive	0	1 (4%)	0	1(1%)
ADHD	0	0	1 (4%)	1(1%)
Burn	0	0	1 (4%)	1(1%)
Totals	28	28	28	84

Bold cells indicated the highest number of responses. Please note that some of the TD children did have medical conditions.

Medical conditions varied across the CI and AI groups (Table 4-3). Cerebral Palsy and children with respiratory illness (asthma, bronchiectasis and cystic fibrosis) accounted for the highest number of CI children and children with congenital heart disease and neurological conditions accounting for the largest number of AI children. The TD reported no known problems except for one child with Attention Deficit Hyperactive Disorder (ADHD) and another with a recent burn.

4.5.2 Dimensions



	AI 1*	AI 2*	AI 3*	CI 1*	CI 2*	CI 3*	TD 1*	TD 2*	TD 3*
Mob	12	6	10	14	2	12	23	3	2
SC	7	1	20	12	6	10	9	8	11
UA	12	7	9	15	8	5	24	2	2
PD	16	9	3	22	6	0	22	5	1
WSU	17	6	5	24	3	1	20	6	2

Figure 4-1 Dimension Responses Across Condition Groups

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems*

Chi-sq and P value: Mobility (15, 0.005); SC (12, 0.017); UA (14, 0.009; PD (7, 0.147); WSU (6, 0.223)

The dimensions of Mob (Chi-sq= 15, p=0.005); SC (Chi-sq=12, p=0.017) and UA (Chi-sq=14, p=0.009) had significant Chi-square results indicating that they differed by condition and that Mob, SC and UA were not independent of condition (Figure 4-1). The children in the AI and CI reported the most problems for the dimensions of Mob, SC and UA (Figure 4-1). However, it can be seen that the caregivers of the AI children reported more a lot of problems in every dimension, whereas, apart from SC, the TD children reported to have the least a lot of problems.

Table 4-4 Dimension Answers According to Age Groups

Age Group		Mob	SC	UA	PD	WSU
0-1 year (n=12)	No Probs	2	2	4	7	10
	Probs	10	10	8	5	2
1-2 years (n=12)	No Probs	7	0	7	10	10
	Probs	5	12	5	2	2
2-3 years (n=12)	No Probs	8	2	7	7	7
	Probs	4	10	5	5	5
3-4 years (n=12)	No Probs	9	2	11	7	11
	Probs	3	10	1	5	1
4-5 years (n=12)	No Probs	7	7	9	9	8
	Probs	5	5	3	3	4
5-6 years (n=12)	No Probs	6	6	3	9	8
	Probs	6	6	9	3	4
6-7 years (n=12)	No Probs	10	9	10	11	7
	Probs	2	3	2	1	5
		40	42	23	10	17
		0.001	***<0.001***	0.300	0.641	0.164

The Chi-squared results indicated that the dimensions answers of Mob (chi-sq=40, p=0.001) and SC (chi-sq=42, p=<0.001) differed with age (Table 4-4) and that Mob and SC were not independent of age. In the 0-1 year category, almost every caregiver reported problems with Mob and SC. SC continued to be reported as a lot of problems in both the 2-3 years and 3-4 years age categories.

Table 4-5 Comparison of Child to Their Normal Behaviour or to Other Children According to Dimension

Dimensions	**Comparison of Behaviour**	**AI** (n=28)	**CI** (n=28)	**TD** (n=28)	**Total** (n=84)	**Chi-sq**	**p-value**
Mob	Own Normal	16(57%)	19(68%)	9(32%)	44 (52%)	9.6	***0.045***
	Others	12(43%)	9(32%)	19(68%)	40 (48%)		
SC	Own Normal	19(68%)	16(57%)	16(57%)	51(61%)	0.9	0.634
	Others	9(32%)	12(43%)	12(43%)	33(39%)		
UA	Own Normal	20(71%)	17(60%)	12(43%)	49(58%)	4.8	0.089
	Others	8(29%)	11(30%)	16(57%)	35(42%)		
PD	Own Normal	26(93%)	28(100%)	27(95%)	81(96%)	2.9	0.240
	Others	2(6%)	0	1(5%)	3(4%)		
WSU	Own Normal	24(86%)	26(93%)	23(82%)	73(87%)	1.6	0.458
	Others	4(14%)	2(6%)	5(18%)	11(13%)		

Chi-squared results indicated that Mob differed by condition groups and that Mob was not independent of condition group (chi-sq = 9.6, p=0.045) (Table 4-5) with most TD children being compared to other children and most CI children being compared to normal behaviour (Table 10). UA was not significant but had the same trend when compared to others. Within the dimensions of Mob, SC and UA the total count between comparison to normal behaviour and other children is similar. The dimensions of PD and WSU are most often compared to the child's own behaviour than to that of other children.

Table 4-6 Comparison of Child to Their Normal Behaviour or to Other Children According to Age Groups

Dimension	**Comparison of Behaviour**	**Age Group**									
		0-1 (n=12)	**1-2** (n=12)	**2-3** (n=12)	**3-4** (n=12)	**4-5** (n=12)	**5-6** (n=12)	**6-7** (n=12)	**Total** (n=84)	**Chi-sq**	**p-value**
Mob	Own Normal	7	6	4	5	5	7	10	44 (52%)	12.1	0.435
	Others	5	6	8	7	7	5	2	40 (48%)		
SC	Own Normal	8	4	6	7	10	8	8	51 (61%)	7.7	0.260
	Others	4	8	6	5	2	4	4	33 (39%)		
UA	Own Normal	8	4	9	4	9	9	6	49 (58%)	11.6	0.084
	Others	4	8	3	8	3	3	6	35 (42%)		
PD	Own Normal	11	11	11	12	12	12	12	81 (96%)	5.2	0.514
	Others	1	1	1	0	0	0	0	3 (4%)		
WSU	Own Normal	9	11	11	10	11	11	10	73 (87%)	2.6	0.862
	Others	3	1	1	2	1	1	2	11 (13%)		

There was no relationship between age of the children and comparing the child's behaviour to their normal behaviour or to that of others (Table 4-6). It is however, of interest to note that the dimensions of PD and WSU were most often compared to the child's normal behaviour. SC also had a higher number of observations based on the child's normal behaviour. Mob and UA were more evenly spread between comparison to others and the child him/herself.

Table 4-7 Perceived Importance of HRQoL Dimensions as Rated by Caregivers According to Condition Groups

Dimension	**Importance**	**Condition Groups**					
		AI (n=28)	**CI** (n=28)	**TD** (n=28)	**Total** (n=84)	**Chi-sq**	**p-value**
Mob	No	4(14%)	3(11%)	1(4%)	8(10%)	2.17	0.338
	Yes	24(86%)	25(89%)	27(96%)	76(90%)		
SC	No	5(48%)	11(39%)	9(32%)	25(30%)	3.32	0.189
	Yes	23(52%)	17(61%)	19(68%)	59(70%)		
UA	No	2(7%)	1(4%)	0	3(4%)	2.85	0.241
	Yes	26(93%)	27(96%)	28(100%)	81(96%)		
PD	No	1(4%)	1(4%)	0	2(2%)	1.65	0.439
	Yes	27(96%)	27(96%)	28(100%)	82(98%)		
WSU	No	0	2(7%)	2(7%)	4(5%)	3.34	0.188
	Yes	28(100%)	26(93%)	26(93%)	80(95%)		

Chi-squared results showed that the relevance of the dimension for HRQoL did not differ according to the condition groups and thus the importance of the dimensions was independent of condition groups (Table 4-7). Mob did however have the highest count of caregivers who perceived Mob as not being important for HRQoL.

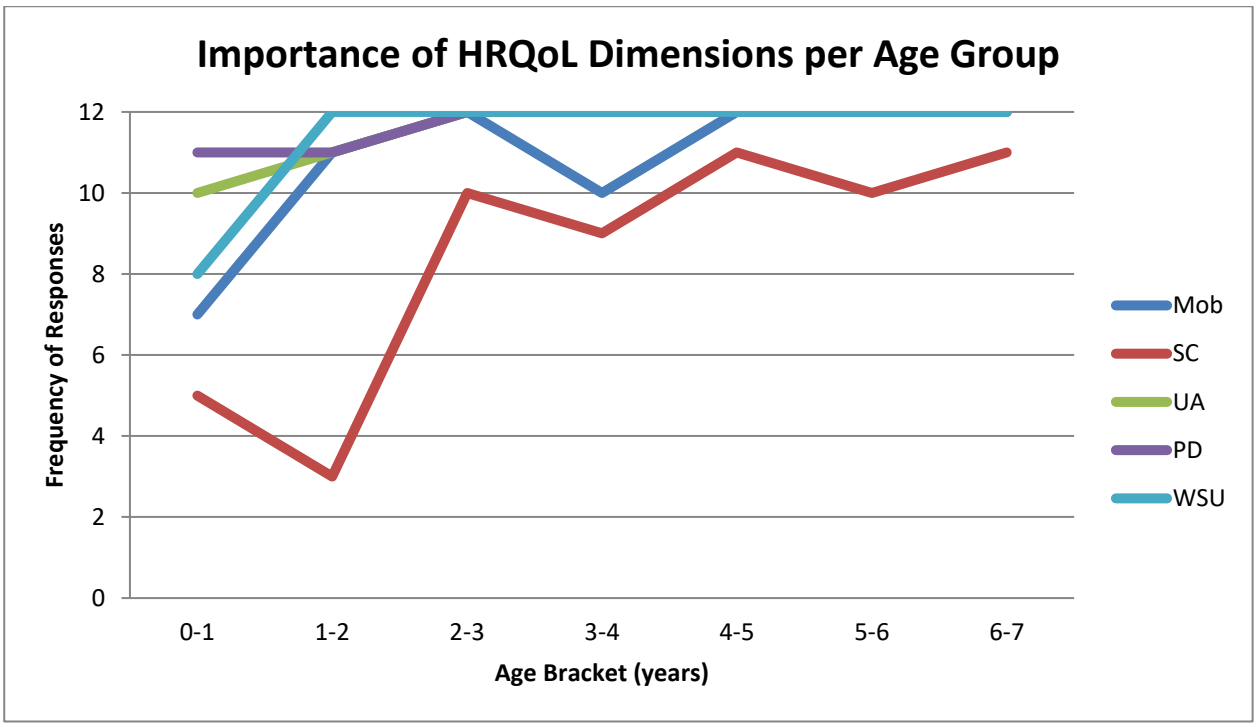


Figure 4-2 Importance of HRQoL Dimensions per Age Group

The chi-squared results indicated that the importance of the dimensions of Mob (chi-sq=18.84, p=0.004); SC (chi-sq=23.59, p<0.01) and WSU (chi-sq=16.89, p=0.009) differed by age (Figure 4-2). Age was found to be independent of UA (chi-sq=8.19, p=0.225) and PD (chi-sq=5.14, p=0.53). The Mob dimension appears to only become important after one year of age and peaks at 2-3 years (Figure 4-2). The importance of SC becomes evident only after 2-3 years of age. WSU similarly peaks at the 1-2 year age group.

4.5.3 Cognitive Debriefing

4.5.3.1 Mobility Dimension

Most caregivers of children aged 0-1 years felt that this was an inappropriate dimension and scored their child as being unable to walk (Appendix 7, Table 10-3). This was attributed to the fact that most children under the age of one year were not yet able to walk. Children who were scored as having no problem with walking were older and were already walking or cruising. Most caregivers felt that this was still an important concept of HRQoL but suggestions were made to classify Mob as the ability to move rather than walking for this age group. Most children aged 1-2 years were scored as being able to walk suggesting that this was an appropriate description of Mob for this age group (Appendix 7, Table 10-4). The problems with walking experienced by children could be attributed to deterioration in function due to acute illness or a chronic condition affecting motor function. Caregivers did however feel that the burden of care of a child

not being able to walk increases with age as young children can play on the floor or be carried around easily. They further identified a link between Mob and development in other dimensions such as schooling, learning and play. There was an association between caregivers of children with chronic conditions not comparing their child to others, they seemed to see their child as an individual and liked to compare their improvement from day to day.

Higher functioning Mob such as running and moving effectively and efficiently became more evident in children between the ages of 2-3 years (Appendix 7, Table 10-5). There was a perceived link by caregivers between one's ability to walk, play, interaction with others and eating, although caregivers of CI children felt that children who were not able to walk could still have fun, play and have a good QoL. Thus the suggestion was made that we observe children's ability to play and have fun rather than walk. There was a strong comparison of their abilities with other children of the same age.

Young children between 3-4 years suffering chronic conditions were suggested to be content and determined with independent mobility being classified as more important than walking (Appendix 7, Table 10-6). It was again proposed that this affects the parent emotionally more than the child. Many believe it is important to know the quality of movement of a child so that they can seek help if not performing the same as peers.

Caregivers of all children aged 4-5 years felt that Mob was a fundamental aspect of HRQoL in children aged 4-5 years (Appendix 7, Table 10-7). They further suggested that Mob helps children to learn independence in life in a time where they are developing a free-will. Learning is aided by the child's curiosity with the desire to explore, discover and play. There was a stronger emergence of socialization, group activities and the ability to keep up with their peers. With this came an emotional connection with Mob for both the parent and the child.

Caregivers reported that children aged 5-6 years had reached a maturity in age and with this they seem to have developed more of an awareness of body limitation and their acceptance among peers became more important (Appendix 7, Table 10-8). Emphasis was placed on peer interaction, schooling, group activities, play and appearance of gait or function. There was again an apparent link between independent Mob and function for schooling, SC, UA and WSU. Most children were able to walk with no problems by the age of 6-7 years; except for two who had problems with clumsiness and a mother's limitation for infection control (Appendix 7, Table 10-9). Walking was deemed very important for HRQoL by all caregivers who justified it with a strong link to independence and to the dimension of WSU. The majority of caregivers thought of their child's normal behaviour as they either considered their child as normal or wanted to monitor their

child's own condition and improvement. Running, jumping and playing were the most observed behaviour in this age group showing the evolution of gross motor skills.

Table 4-8 Frequency of Reasons for Scores for Mob Dimension Across Age Groups

Mob	**0-3yrs** (n=42)	**4-7yrs** (n=42)	**Total** (n=84)
Normal- functions with activity deemed 'normal' or similar to others	12 (29%)	30 (71%)	42(50%)
Unable - unable to carry out function due to age, health or disability	6 (14%)	4(10%)	10(12%)
Running - higher function than walking	3(7%)	7(17%)	10(12%)
Different - not within normal parameters but achieves task	0	8(19%)	8(10%)
Age - not appropriate function for age of child	7(17%)	0	7(8%)
Trying - not age appropriate or with normal pattern but attempting task partially or assisted.	3(7%)	4(14%)	7(8%)
Balance - difficulty with balance	0	4(10%)	4(5%)
Able – able to perform all tasks	3(7%)	0	3(4%)
Crawling – ability to move through crawling	2(5%)	1(2%)	3(4%)
Delayed - developmental milestones are delayed	3(7%)	0	3(4%)
Moves- not normal mobility for age (walking) but is able to move to get where they want to be	2(5%)	1(2%)	3(4%)
Assistive device- achieved with assistance from an external aid	0	2(5%)	2(2%)
Illness - illness affects all or partial function	1(2%)	1(2%)	2(2%)
Tires- Able to perform activity but limited as tires easily	0	1(2%)	1(1%)
Climbs - ability to climb under or over object	0	1(2%)	1(1%)
Healthy - without illness or disability	0	1(2%)	1(1%)
Independent - important for developing Independence	1(2%)	0	1(1%)
Play- important for play	0	1(2%)	1(1%)
Pre-morbid- pre-morbid function normal or condition changed due to health	1(2%)	0	1(1%)
Shakes- muscles or body shaking or swaying with change in posture	0	1(2%)	1(1%)
Worry- child's concern about inability	0	1(2%)	1(1%)
Advanced- more advanced than other children of the same age	1(2%)	0	1(1%)
Enjoys - child enjoys the function	0	1(2%)	1(1%)
Hospitalised- unable to achieve task due to hospitalisation	0	1(2%)	1(1%)
Pain – limited by pain	0	1(2%)	1(1%)

The analysis of results in two larger age groups of 0-3 years and 4-7 years was as a result that the importance of the dimensions of Mob, SC and UA all peaked at 2-3 years (Table 4-8). Results from the cognitive debriefing could thus suggest the reasoning behind this shift in importance.

Agreement between two independent researchers for the coding of reasons for answers given for the dimension of Mob was 92%. The remaining descriptors were discussed until agreement could be found.
Despite the large number of a lot of problems in Mob in the younger age categories, children were still most often perceived by their caregiver as being 'normal' in terms of mobility. Children under the age of three years were perceived most often as being unable to fulfil the task due to their age or other health reason. Children over the age of three years were thought of as having a higher function than walking. It also became more apparent that children deviate from normal or are 'different' in this very young age group (0-3 years).

4.5.3.2 Self -Care Dimension

Caregivers did not feel that this was an appropriate description of SC for children between 0-2 years of age as they were too young to wash or dress themselves and were dependent on their caregivers for both tasks (Appendix 7, Table 10-10 and Table 10-11). Some identified that all children had some level of SC which differed across age groups. More appropriate items for SC were suggested as the child's ability to eat, sleep well, play and communicate their needs. In addition to these items for children closer to two years of age there was an emergence of potty training.

Children aged 2-3 years seemed to be actively learning and participating in the process of washing and dressing (Appendix 7, Table 10-12). However, most of the responsibility of both tasks remained with the caregivers. Although the concept of SC was important due to implications for learning and independence children of this age would not seemingly be impacted by not being able to wash or dress independently. A more important focus in this age group would be assisting with these SC tasks as well as independent eating, communicating needs and potty training.

Assisting with washing and dressing was important for the development of independence and showed an ability to learn and foster self-pride in children aged 3-4 years (Appendix 7, Table 10-13). Children still needed supervision but seemed to be taking on more responsibility for the task. The concept of SC was still mostly thought to be important but that the question should put emphasis on the assistance with SC activities rather than independent completion. The development of independence was a strong theme in

this age group and may warrant more emphasis. Potty training could perhaps be another example of learning and the development of independence.

The differences in HRQoL, with regard to SC, became more apparent with TD children only needing supervision with washing and dressing from 4-5 years of age (Appendix 7, Table 10-14). Acute illness showed deterioration in abilities with SC whereas chronic illness showed long term difficulties with care. The difficulties children had at this age were: fine motor skills such as zips, laces and buttons and thorough washing. One would not normally observe other children washing and dressing thus this was rated on the child's normal behaviour or compared to that of a sibling. Again learning independence with washing and dressing was the most important aspect contributing to HRQoL.

There was a difference in ability between AI, CI and TD children aged 5-6 years (Appendix 7, Table 10-15). Taking into account that one of the TD children had burnt her leg, they otherwise all showed no problem with SC tasks. On the contrary most of the AI children were unable to wash and dress whilst some of the CI children showed difficulty. Most caregivers felt that this was an important function at this age – showing development and independence. Behaviour was mostly compared to that of the child as they were previously able to complete the task or there were no concerns with their development.

There was one TD child aged 6-7 years who scored a lot of problems with SC. He had been diagnosed with ADHD and spatial relation problems which accounted for his difficulties. The children reporting some problems were both appropriate due to anxiety with hospitalisation and problems with fine motor skills due to chronic illness. Again most caregivers compared the tasks "today" to the child's normal behaviour due to the limited exposure to other children or accepting their child for who they were (Appendix 7, Table 10-16).

The answers seen in Table 4-9 below reflect that SC is seen as an inappropriate function for children under three years of age and remains the responsibility of the caregiver. In children over three years of age they are seen as carrying out the function normally or learning to do the task in an age appropriate manner. Agreement between two independent researchers for the coding of reasons for answers given for the dimension of SC was 89%. The remaining descriptors were discussed until agreement could be found.

Table 4-9 Frequency Table of Reasons for Answers on the SC Dimension Across Age Groups

SC	**0-3yrs** (n=42)	**4-7yrs** (n=42)	**Total** (n=84)
Age- not appropriate function for age of child	29 (69%)	7(17%)	36(43%)
Normal- functions with activity deemed to be 'normal' or similar to others	1(2%)	19(45%)	20(24%)
Learning- learning to do task in age appropriate manner	4(10%)	10(24%)	14(17%)
Unable- unable to carry out function due to age, health or disability	4(10%)	6(14%)	10(12%)
Caregiver- role of the caregiver	8(19%)	2 (5%)	10(12%)
Trying- not age appropriate or with normal pattern but attempting task partially or assisted	3(7%)	6(14%)	9(11%)
Pre-morbid- pre-morbid function normal or condition changed due to health	2 (5%)	2 (5%)	4(5%)
Independent- important for developing Independence	0	3(7%)	3(4%)
Attention- attention seeking behaviour	0	1(2%)	1(1%)
Attitude- poor attitude toward task	0	1(2%)	1(1%)
Enjoy- child enjoys the function	1(2%)	0	1(1%)
Verbalise- verbalise his/her own state	0	1(2%)	1(1%)

4.5.3.3 Usual Activities Dimension

Play was a reoccurring theme among children aged 0-1 years of age (Appendix 7, Table 10-17). Play was seen by caregivers as important for cognitive learning, interaction with others, gross motor and fine motor skills. Some of the caregivers took the examples on this question as criteria to fulfil in determining the child's ability resulting in a high number of children having some or a lot of problems with UA. Play was thought to have an important impact on HRQoL although this may be more apparent at an older age and had more effect on the parent than the child. When caregivers reported the reasoning that the dimensions was important many of them expressed that it was more important for them to see their child play. Play in the young child was seen as less important. Other important items which were suggested included: play only, socializing, communication, eating and sleeping.

Play was again identified as the most important UA for children aged 1-2 years (Appendix 7, Table 10-18). There was an observed difference in play with better ability in TD than AI and CI children. The association between ability to play and emotions was suggested. Play was thought to be important for development of skills as well as learning and independence.

This was considered an important dimension for children aged 2-3 years as the activities were considered meaningful for children as they learn and develop social bonds through play (Appendix 7, Table 10-19). It was postulated that children wanted to perform similarly to their peers. If unable to perform similarly to

peers it would have emotional consequences. Furthermore, there were observed difference with AI and CI children having higher reported problems with UA than TD

Attendance at school was emerging to as important for children aged 3-4 years (Appendix 7, Table 10-20). Engaging with friends and playing with others was important for learning. Family was considered an important part of the child's life as there were no close friendships yet at this age. These activities were highly observable and were mostly compared to that of other children.

Considering the age group of 4-5 years none of the caregivers who reported that the AI children had no problems with UA took into account the activities mentioned or the time frame of today (Appendix 7, Table 10-21). For one of the CI children environmental factors limited participation in UA. UA were considered important by all caregivers with its strong link to learning, independence and emotions.
There was a difference in ability to participate in UA between the TD and the AI and CI group in children aged 5-6 years (Appendix 7, Table 10-22). School was beginning to become more important in this age group and play remained important with its influence on learning. There were no suggested alternate items for this age group.

There were very few reported problems with UA with the AI group in children aged 6-7 years (Appendix 7, Table 10-23). When asked for the rationale behind the answers it was apparent that the hospital environment was very supportive to AI children and offered schooling and encouraged normal activities. It was also clear that the time frame of 'today' was not always considered with one caregiver scoring the child with no problems with the reasoning that if his child were not in hospital it would not be a problem. The CI group was very well supported in their respective environments at home with adaptations allowing for their full function.

Many children were deemed to be Normal within the UA dimension with children in the 4-7 year age category having a higher frequency than children in the 0-3 year age category (Table 4-10). It was clear that many of the descriptors under UA were not deemed appropriate for children under the age of three years. The environment became an important factor in the older age group which would either assist or hamper UA. Agreement between two independent researchers for the coding of reasons for answers given for the dimension of UA was 96%. The remaining descriptors were discussed until agreement could be found.

Table 4-10 Frequency Table of Reasons for Answering UA Dimension Across Age Groups

UA	**0-3yrs** (n=42)	**4-7yrs** (n=42)	**Total** (n=84)
Normal- functions with activity deemed to be 'normal' or similar to others	17(40%)	23(55%)	40(48%)
Age- not appropriate function for age of child	14(33%)	0	14(17%)
Environment- environmental factors inhibit or enable function	1(2%)	12(29%)	13(15%)
Unable- unable to carry out function due to age, health or disability	3(7%)	7(17%)	10(12%)
Trying- not age appropriate or with normal pattern but attempting task partially or assisted	4(10%)	4(10%)	8(10%)
Pre-morbid- pre-morbid function normal or condition changed due to health	2(5%)	2(5%)	4(5%)
Tires- able to carry out task but tires easily	0	4(10%)	4(5%)
Enjoys- child enjoys the function	2(5%)	0	2(2%)
Limited- able to carry out function but limited by health condition	1(2%)	1(2%)	2(2%)
Anxiety- anxiety keeps child back from certain activities	1(2%)	0	1(1%)
Cognition- higher mental function	0	1(2%)	1(1%)
Different- not within normal parameters but achieves task	1(2%)	0	1(1%)
Frustrated- frustrated and not achieving task	0	1(2%)	1(1%)
Illness- illness affects all or partial function	0	1(2%)	1(1%)
Knowledge- develops the child's knowledge	0	1(2%)	1(1%)
Reference- child carries out his/her normal function as opposed to how other children carry them out	0	1(2%)	1(1%)
Scared- scared to carry out function	1(2%)	0	1(1%)

4.5.3.4 Pain or Discomfort Dimension

For the age group 0-2 years AI children were reported as having PD whereas CI and TD were not (Appendix 7, Table 10-24 and Table 10-25). Discomfort was not clear to all the caregivers and it was suggested to include Pain only. CI children were compared to themselves as all of the caregivers felt that they knew their child's behaviour and condition. There were many observable behaviours on which the caregivers based their answer. PD seemed to have links to UA (play), WSU (happy) as well as the ability to sleep and eat.

Pain was thought of by one of the caregivers of a child in the 2-3 year age group as an emotional concept where the child was in pain when his mother left for work in the morning (Appendix 7, Table 10-26). Another caregiver assumed that there must have been pain as the child was sick. Other caregivers based their answer on observable behaviour with good descriptions of pain behaviour. Pain was thought to affect sleep, interaction with others, mobility, appetite, play, emotions and general development. As with other age groups there were some caregivers who did not understand discomfort and felt that the dimension should include only pain.

Similar to the younger age group caregivers of children aged 3-4 years assumed pain due to hospitalisation or the presence of an attachment such as a drip (Appendix 7, Table 10-27). Pain was again attributed to emotions with the child not knowing his father. Children seem to have verbalised pain well at this age. The effects of pain on school, learning and concentration emerged at this age.

PD was distributed equally among AI, CI and TD children aged 4-5 years (Appendix 7, Table 10-28). Discomfort from a dirty nappy and pain from head and stomach aches contributed to some of the PD. The effects of PD on other dimensions emerged again. A caregiver of a CI child highlighted that a child with a disability is often assumed to be suffering and in pain but the contrary is true.

Caregivers of children aged 5-6 years relied on their child's ability to verbalise their PD (Appendix 7, Table 10-29). In this age group one of children the TD child had lots of PD as she had suffered a burn to the leg in the previous week. The link to other dimensions was again apparent. PD became a much clearer dimension the older the child got with the presence of pain being less frequently reported in children 6-7 years (Appendix 7, Table 10-30). This was deemed as an important dimension for the impact it had on other dimensions.

Table 4-11 Frequency Table of Reasons for Answering PD Dimension Across Age Groups

PD	**0-3yrs** (n=42)	**4-7yrs** (n=42)	**Total** (n=84)
Content- awake/asleep happily with normal function	17(40%)	13(31%)	30(36%)
Verbalise- verbalise his/her own state	4(10%)	25(60%)	29(35%)
Illness- illness affects all or partial function	3(7%)	7(17%)	10(12%)
Healthy- without illness or disability	0	7(17%)	7(8%)
Situation- the situation deems that the child is in pain	6(14%)	1(2%)	7(8%)
Discomfort- uncomfortable due to internal or external factors	2(5%)	1(2%)	3(4%)
Crying- a different type of crying	2(5%)	0	2(5%)
Emotional- emotional/psychological wellbeing	0	2(5%)	2(5%)
Restless- uncomfortable movement	1(2%)	1(2%)	2(5%)
Intuition- intuition of a parent	1(2%)	0	1(1%)
Observe- ability to see function or task	0	1(2%)	1(1%)
Seizures	1(2%)	0	1(1%)
Unknown	1(2%)	0	1(1%)

Agreement between two independent researchers for the coding of reasons for answers given for the dimension of PD was 87%. The remaining descriptors were discussed until agreement could be found.

When asked about PD most caregivers classified their child as being happy or content and therefore without pain. It became apparent that from the age of four years children are far more articulate and are able to verbalise the presence of pain (Table 4-11).

4.5.3.5 Worried, Sad or Unhappy Dimension

Children under one were thought to be too young to feel WSU by some of the caregivers and it was suggested that it affected the parent more than the child (Appendix 7, Table 10-31). The reason given for TD children experiencing some problems with WSU was that the child was hungry. CI children were all rated as happy with one caregiver guessing and another expressed that her child showed no emotions. Some of the caregivers recommended that the dimension was removed. Suggestions for alternative dimensions included: growth, eating, sleeping and cognition.

For children aged 1-2 years there was an assumption with an AI child that he must be WSU as he was sick (Appendix 7,Table 10-32). There was a suggested link between WSU and playing, learning and development. The dimension was poorly understood for caregivers of children aged 2-4 years (Appendix 7, Table 10-33). One of the caregivers had linked worry with separation anxiety in her child. The other caregivers felt that this dimension became more important the older the child became. The only child experiencing problems with WSU in the 3-4 year age group was TD and was said to get upset when his mother left for work (Appendix 7, Table 10-34). It was suggested by some to remove the dimension entirely and others suggested that the word “worried” be removed.

The problems reported with children in the CI and TD aged 4-5 years in the WSU dimension were associated with the child wanting to go home whilst waiting for a clinic visit and another child missing a father who was absent in her life (Appendix 7, Table 10-35). The vocalisation of emotions seemed to develop at this age. One of the caregivers suggested that the question be reworded positively and asked about happiness rather than unhappiness. A caregiver of a child aged 5-6 years suggested that worried and unhappy be removed from the question (Appendix 7, Table 10-36).

Caregivers from the 6-7 year age group had again suggested that WSU may affect children more later in life than at this age and that it may have more of an effect on the caregiver than the child (Appendix 7, Table 10-37). It was thought by others to affect self-confidence and overall functioning. The CI child reported as experience worry wanted to stay with her grandmother and one of the TD children was worried as her mother had to leave for work. The other TD child had ADHD and had poor school performance and worried about being reprimanded.

Table 4-12 Frequency Table of Reasons for Answering WSU Dimension Across Age Groups

WSU	**0-3yrs** (n=42)	**4-7yrs** (n=42)	**Total** (n=84)
Happy- child is content	11(26%)	10(24%)	21(25%)
Vocalise- verbalise his/her own state	0	12(29%)	12(14%)
Behaviour- indicates whether there is any emotional change	4(10%)	3(7%)	7(8%)
Intuition- intuition of a parent	2(5%)	4(10%)	6(7%)
Play- important for play	4(10%)	2(5%)	6(7%)
Cry- different cry	1(2%)	3(7%)	4(5%)
not appropriate- not appropriate for child's age	1(2%)	3(7%)	4(5%)
Sickness- presence of any illness	3(7%)	1(2%)	4(5%)
Smiling- child is smiling	3(7%)	1(2%)	4(5%)
Anxiety- anxiety causing the child emotional changes	1(2%)	1(2%)	2(2%)
Excited- Child is excited	1(2%)	1(2%)	2(2%)
Guessed- The answer was guessed	2(5%)	0	2(2%)
Upset- child is upset	0	2(5%)	2(2%)
Unhappy- child is unhappy	1(2%)	0	1(1%)
abnormal behaviour – behaviour deviating from normal	1(2%)	0	1(1%)
Chatty- talking	0	1(2%)	1(1%)
Clingy- wants to be with caregiver at all times	0	1(2%)	1(1%)
frustrated - frustrated and not achieving task	0	1(2%)	1(1%)
Healthy - without illness or disability	1(2%)	0	1(1%)
Hungry- concerned as child is hungry	1(2%)	0	1(1%)
Laughing- child is laughing	1(2%)	0	1(1%)
Moody- child's mood is different to normal	0	1(2%)	1(1%)
Pain- presence of pain is causing emotion	1(2%)	0	1(1%)
Parent- parent is more emotional than the child	1(2%)	0	1(1%)
Scared- child is scared of the hospital	0	1(2%)	1(1%)
supportive environment – create a supportive environment which allows child to accept her condition	0	1(2%)	1(1%)

Agreement between two independent researchers for the coding of reasons for answers given for the dimension of WSU was 86%. The remaining descriptors were discussed until agreement could be found. Table 4-12 shows that children were most often described as being happy in both age groups. There was a distinct difference in children over four years of age being able to articulate their feelings.

4.5.4 The Visual Analogue Scale

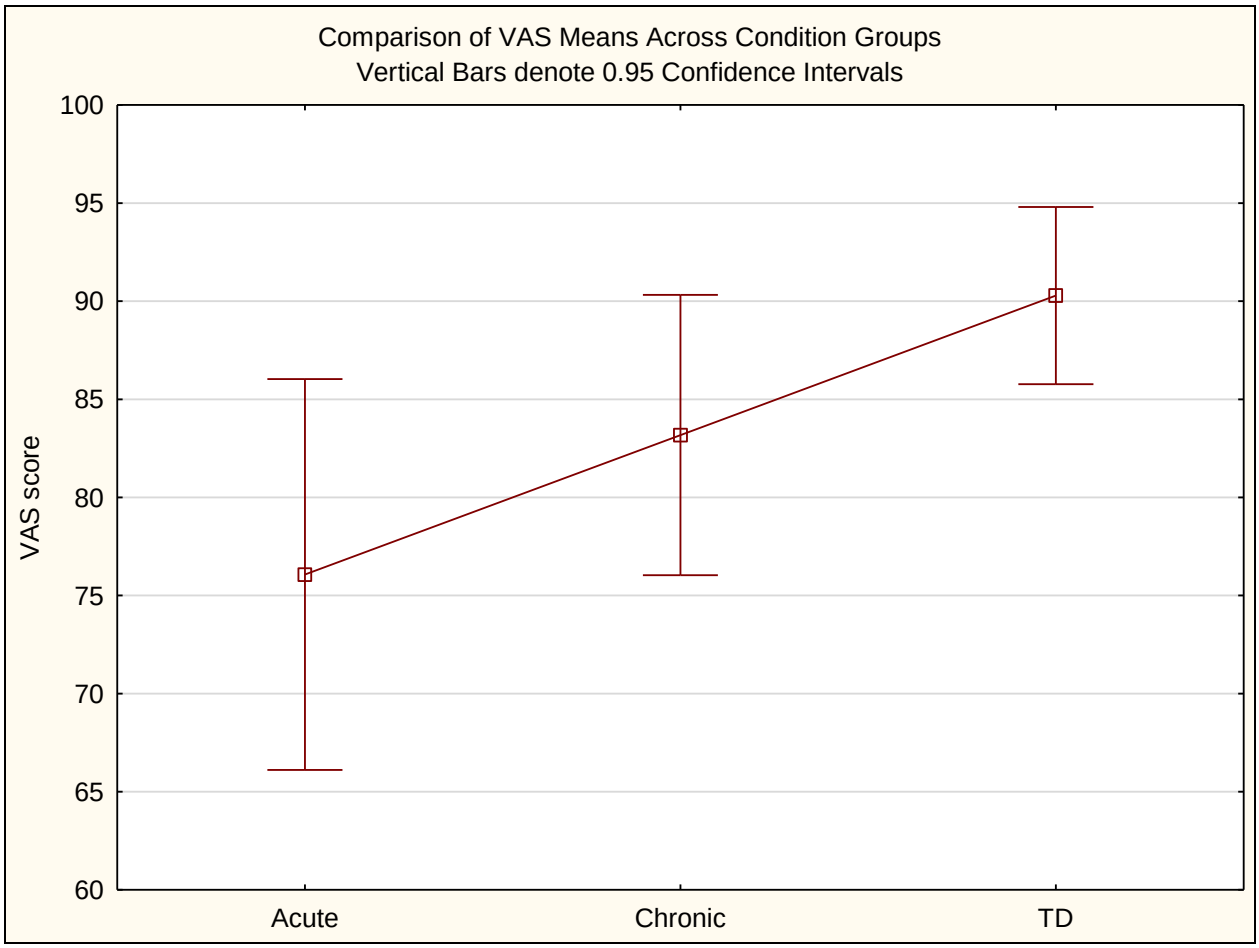


Figure 4-3 Comparison of VAS Means Across Condition Groups

Current effect: F (2. 81) =3.97, p=0.02

There was a significant difference (p=0.02) between condition groups (Figure 4-3). AI was the lowest ranked (mean=76; std dev=25) (IQR 0-100), CI (mean=83; std dev= 18) (IQR 35-100), AI (mean=90; std dev=11) (IQR 60-100). Post Hoc Tukey Analysis (Table 4-13) indicated that AI was significantly different from TD (p=0.02) and CI was not different to either of them.

Table 4-13 Post Hoc Analysis of VAS mean results across condition groups

Condition Group	Mean VAS Score	1*	2*	3*
AI	76.1		0.4	*0.02*
CI	83.2	0.4		0.4
TD	90.3	*0.02*	0.4	

1 No problem in dimension; 2* 2* problems in dimension; 3* problems in dimension*

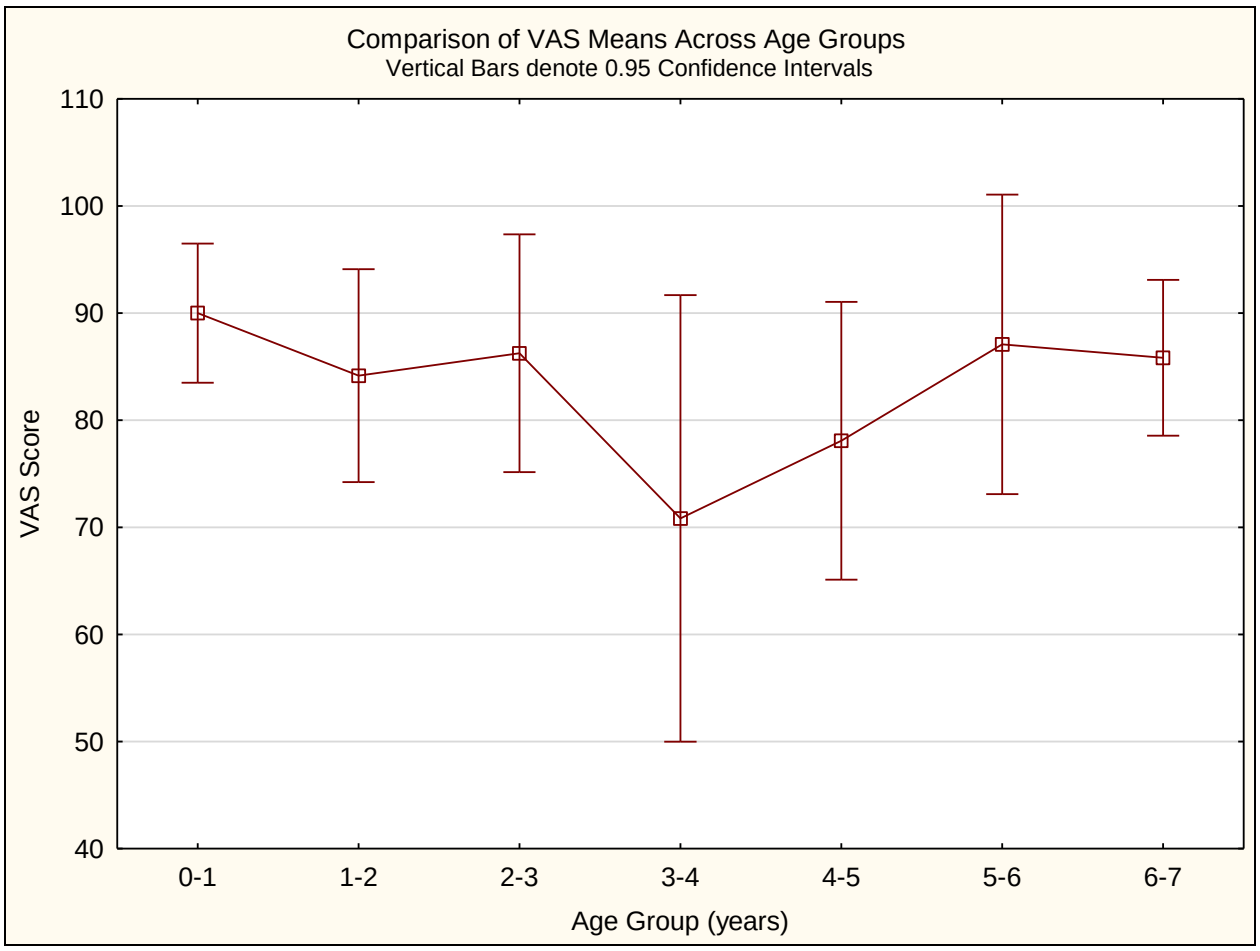


Figure 4-4 Comparison of VAS Means Across Age Groups

Current effect: F (6.77) =1.30. p=0.265

No significant difference of VAS means across the age groups (p=0.265) as the 95% confidence intervals all overlap (Figure 4-4).

Regression analysis was performed with the VAS as dependent variable and dummy variables created to represent some problems and a lot of problems in each of the dimensions. Residual Analysis was performed to identify the participants whose scores were >2 standard deviations between predicted and observed. Three outliers were excluded and the Adjusted R^2=0.075 increased to Adjusted R^2=0.12 (Table 4-14). None of the dimensions significantly predicted the VAS score, apart from WSU 2* (approached significance p=.052) and 3* (p=.017) which decreased the VAS by 11 and 16 respectively. Mob 3*, SC 2*, UA 3* and PD 2* all counterintuitively increased the VAS score.

Table 4-14 Regression Analysis of VAS for all Children and Age Groups

	b*	Std. Err. of b*	b	Std. Err. of b	t(70)	p-value
Intercept			90.57	3.41	26.58	0.000
Mobs 2*	-0.14	0.12	-6.61	5.75	-1.15	0.255
Mob 3*	0.12	0.14	4.34	4.98	0.87	0.387
SC 2*	0.03	0.12	1.08	5.15	0.21	0.834
SC 3*	-0.14	0.13	-4.53	4.20	-1.08	0.285
UA 2*	-0.10	0.13	-4.12	5.09	-0.81	0.421
UA 3*	0.09	0.14	3.42	5.73	0.60	0.553
PD 3*	0.02	0.13	0.73	5.01	0.15	0.884
PD 2*	0.05	0.13	3.83	10.78	0.36	0.723
WSU 2*	-0.26	0.13	-10.71	5.40	-1.98	*0.052*
WSU 3*	-0.30	0.12	-16.28	6.68	-2.44	***0.017***

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension Adjusted R^2=0.12 (n=81)*

The model when applied to all children did not fit the data well and accounted for only 12% of the variance. Further regression was done to see if the dimension scores accounted for more variance in children younger and older than three years. The cut-off point of three years was chosen due to the fact that both Mob and SC emerge as important after this age. In the younger children no outliers were identified and the Adjusted R^2=0.24 (Table 4-15). A lot of pain and discomfort (p=0.023) was found to significantly predict VAS.

Table 4-15 Regression Analysis of VAS for Children Under Three Years of Age

	b*	Std. Err. of b*	b	Std. Err. of b	t(17)	p-value
Intercept			97.18	7.15	13.60	0.000
Mobs 2*	-0.09	0.17	-7.72	14.20	-0.54	0.592
Mob 3*	0.23	0.21	6.28	5.72	1.10	0.283
SC 2*	-0.32	0.22	-10.67	7.29	-1.46	0.156
SC 3*	-0.25	0.22	-7.57	6.66	-1.14	0.267
UA 2*	0.47	0.25	14.49	7.60	1.91	0.069
UA 3*	0.05	0.22	2.76	13.18	0.21	0.836
PD 3*	-0.60	0.25	-19.63	8.11	-2.42	***0.023***
PD 2*	-0.30	0.21	-25.00	17.31	-1.44	0.162
WSU 2*	-0.05	0.22	-2.26	11.08	-0.20	0.840
WSU 3*	-0.25	0.21	-8.65	7.25	-1.19	0.244

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension Adjusted R^2=0.24 (n=35)*

In the older children one outlier was excluded and the model fit the data better, accounting for 28% of the variance (Adjusted R^2=0.22 increased to Adjusted R^2=0.28) (Table 4-16). The presence of SC 3* reduced VAS by 18 and the PD 3* variable reduced it further by 36.5. In contrast UA 3* increased the VAS by 27.

Table 4-16 Regression Analysis of VAS with Children Over Three Years of Age

	b*	**Std. Err. of b***	**b**	**Std. Err. of b**	**t(36)**	**p-value**
Intercept			90.1	5.08	17.72	0.000
Mob 2*	-0.088	0.156	-4.8	8.43	-0.56	0.576
Mob 3*	0.042	0.149	3.0	10.75	0.28	0.778
SC 2*	0.096	0.146	5.0	7.63	0.66	0.515
SC 3*	-0.370	0.160	-18.3	7.96	-2.30	***0.027***
UA 2*	-0.163	0.140	-9.2	7.92	-1.16	0.253
UA 3*	0.412	0.161	27.4	10.68	2.56	***0.015***
PD 2*	-0.134	0.139	-7.2	7.54	-0.96	0.343
PD 3*	-0.332	0.139	-36.5	15.31	-2.39	***0.022***
WSU 2*	-0.179	0.145	-11.1	9.04	-1.23	0.226
WSU 3*	-0.116	0.142	-7.2	8.86	-0.82	0.419

1 No problem in dimension; 2* problems in dimension; 3* A lot of problems in dimension Adjusted R^2=0.28 (n=47)*

4.5.5 General Questionnaire

The items that could be added to increase the content validity of the new instrument according to age group presented in Table 4-17 below, in decreasing order of frequency.

Table 4-17 Frequency of Items to be Added per Age Group

	Age Group (years)							
	0-1 (n=12)	1-2 (n=12)	2-3 (n=12)	3-4 (n=12)	4-5 (n=12)	5-6 (n=12)	6-7 (n=12)	Total (n=84)
Eating	9	8	5	4	6	4	1	37(44%)
Communication	10	6	3	2	1		1	23(27%)
Movement	12	2	1	2		2		19(23%)
Potty training		2	4	3	3	4		16(19%)
Sleep	7	2	2					11(13%)
Play only	3	1	2			1	2	9(11%)
Walking	2		3	2	2			9(11%)
Discomfort only		1	1	2	3		1	8(10%)
Worried only	1	1	1	1	1	1		6(7%)
Assist with self-care				3		1		4(5%)
Independence			1	1	2			4(5%
Upper limb movement	4							4(5%
Cognition	1			2				3(4%)
Burden of care	1				1			2(2%)
Emotion							2	2(2%)
Kicking	2							2(2%)
Motivation			1			1		2(2%)
Pride and Self-esteem			1	1				2(2%)
Sad		1				1		2(2%)
Senses	2							2(2%)
Socialize	2							2(2%)
Crawling							1	1(1%)
Dependence on Care	1							1(1%)
Growth	1							1(1%)
HIV and TB status					1			1(1%)
Hygiene	1							1(1%)
Immunizations						1		1(1%)
Interaction	1							1(1%)
Parent's HRQoL					1			1(1%)
Perception					1			1(1%)
Positive attitude					1			1(1%)
Routine						1		1(1%)
Rules					1			1(1%)
Security					1			1(1%)
Sickness			1					1(1%)
Worried, sad	1							1(1%)

*N=84, * Caregivers did not all suggest additional items, and some suggested more than one item.*

The highest number of suggested items was in the lower age groups, most notably the 0-1 year group (Table 4-17). Communication and eating were identified as important across all of the age groups.

Movement, as opposed to walking about, was suggested for the age group of 0-1 years. Sleeping was suggested for children in the age band 0-3 years. Potty training emerged as a new item for the age band of 1-6 years. Play as an item on its own, as opposed to a descriptor under UA, was suggested across age groups (Table 4-17).

Table 4-18 Frequency of Items Suggested to be Deleted

Item	**Frequency of suggestion**
Delete Discomfort	8
Delete WSU dimension	6
Delete "Worried" from WSU dimension	5
Delete "about" in "walking about"	4
Delete "Worried" and "Sad" from WSU dimension	3
Delete "Sad" from WSU dimension	2
Delete "Unhappy" from WSU dimension	1

**Not all caregivers suggested an item to be deleted.*

There were few suggestions about items which should be deleted (Table 4-18). Most of the suggestions came for the dimension of WSU where all three constructs were difficult to understand, 'worried' being the most problematic. Further suggestions included the term 'walking about' in the mobility dimension which was suggested should only refer to 'walking'. The word 'discomfort' was poorly understood in PD and was suggested that the dimension only include pain.

Table 4-19 Suggested Layout Changes

Suggestion	**Frequency of suggestion**
Explanation of worst and best health for VAS	9
Explain Health for VAS	8
Add pictures to the VAS	6
Pictures next to descriptions on Dimensions e.g. smiley faces	5
Add descriptions/scenarios to the VAS	3
Today should be emphasized in each question	2
Change the order: PD; WSU; UA; SC and then mobility. Too much emphasis on physical ability	1
Five levels rather than three	1
Quantification of some and a lot	1
Change UA into daily activities or daily interactions	1

**Not all caregivers suggested a layout change.*

There were also very few suggested layout changes (Table 4-19). The majority of suggestions were regarding the VAS to improve the comprehensibility of the question and the concept of health.

4.6 Discussion

The dimension development of HRQoL measures for young children was poorly described in the published literature with lacking a specific conceptual framework or selection of dimensions by a number of stakeholders including parents and children [34], [244] . Whereas it might have been stated that expert opinion was sought or caregivers or children were interviewed, the processes of data attainment for these processes was not well described. This chapter described the next stage of stake-holder consultation in the development of the mooted instrument. The overall aims of this chapter was to establish if the EQ-5D-Y Proxy version had content validity across the age groups and to consult with care-givers regarding the item inclusion, frame of reference and layout with regard to the proposed new questionnaire.

4.6.1 Sample

The sample was stratified according to age group thus there was a good distribution of AI, CI and TD children across each age group. The inclusion of caregivers with children diagnosed with a spectrum of health classifications was important to ensure that the new measure and items were representative of diverse populations for future use. It was also necessary to include children with a range of health conditions to allow for testing of known group validity. The reported health conditions for AI and CI children was diverse and included children with severe physical disability and some who were affected more from a cognitive or respiratory perspective. Only two of the TD children were reported as having a health condition one with ADHD and one with a recent burn. Informants (caregivers) of TD children had a higher formal education level ($p=0.002$) and the results may be biased toward middle class respondents. This may not have influenced the results received as a Swedish study found that caregivers of different education level were in agreement with the impact that nutrition, physical activity, play and social relations had on health [245].

4.6.2 Is the EQ-5D-Y Valid Across Age Groups?

The dimensions of the EQ-5D-Y performed as expected showing differences between known groups with children in the AI and CI reporting the most problems. Caregivers of the AI children reported more a lot of problems in every dimension, whereas, apart from SC, the TD children reported to have the least number of

a lot of problems. This indicated that the dimension of SC does not behave as expected across known groups and the scoring of problems was attributed to an external factor. This external factor was most likely the age of the child as dimension the dimension of SC was associated with age with younger children (0-4 years) reporting more problems. Furthermore, nearly all of the caregivers reported problems with Mob in the 0-1 year category. This could be attributed to the developmental progression of children; tasks such as washing and dressing are complex and use higher cognitive function as well as fine motor skills and body awareness. This typically develops in children after the age of two years [112], [246]. Similarly the skill of walking is generally only attained between 12 and 18 months of age [247].

The rating of general health (VAS) showed known group validity with AI ranked the lowest. AI was significantly different from TD but CI was not different to either of them. Scott et al (2017), found similar results on the VAS score of the EQ-5D-Y is children aged 8-12 years from the same population [248]. There was no significant difference of VAS means across age groups suggesting that the rating of general health performed well across all age groups and conditions.

The dimensions scores were not a good model when applied to all of the children as it only accounted for 12% of the variance in the VAS scores. The model improved somewhat when children were divided into two groups: over three years and under three years of age. The model when applied to children under three years of age accounted for 24% of the variance it performed even better for children over the age of three years of age with the dimension scores accounting for 28% of the variance. The presence of a lot of problems in SC and PD (for children over three years of age) significantly reduced the VAS score; in contrast a lot of problems with UA increased the VAS score. The dimension scores were not predictors of the VAS score (although this was better with older children) and could suggest that dimension revision is necessary for the very young child.

4.6.3 Content Validity of the Items Across Age Groups

There was an association between age and the importance of the dimensions of Mob with the dimension only being perceived as important for children after one year of age. The importance of SC was only perceived as important after 2-3 years of age; similarly children started scoring fewer problems with SC after this age. The perceived importance of the WSU dimension similarly peaked at the 1-2 year age group. Thus the dimensions of Mob, SC and WSU need to be revised for very young children. There was no association between age and the importance of dimensions for either UA or PD. Thus UA and PD would both be important to retain in an instrument for very young children.

There was no association between the importance of dimensions for HRQoL and the condition groups. Mob did have the highest count of caregivers who perceived Mob as not important for HRQoL with higher numbers in AI and CI children. In the younger children, 0-1 year, the Mob dimension was not deemed important but most caregivers felt that the older the child gets the more important it would become. They did however feel that movement would be a better description of Mob than walking for this age group and the importance would then be reconsidered. This was due to the fact that in normal motor development walking is acquired at around 12 months of age [246]. The burden of care was also reported to increase with the child being unable to walk and this burden further increases the older the child becomes.

The dimension of SC was only considered important for children over three years of age. This could be attributed to the developmental progression of children; tasks such as washing and dressing are complex and use higher cognitive function as well as fine motor skills and body awareness. This typically develops in children after the age of two years [112], [246]. The concept of SC was rated as important, by caregivers, due to the implication for learning and independence in children over three years of age. Although if children were unable to perform the task at this age it was not thought to have dire consequences as they would only be assisting with the task.

UA was considered an important dimension by 98% of the caregivers. The descriptor of play under UA was considered as the most important attribute of UA for children. Play was suggested as important for cognitive learning, interaction with others and the acquisition of gross motor and fine motor skills for children under the age of one year. The caregiver's reflection of play is well supported in the literature [112], [246]. Caregivers took examples in the question as criteria to fulfil leading to the younger age group (0-3 years) having a higher report of problems with UA. This further strengthened the suggestions to only include play as a descriptor for UA.

The importance of pain across all age groups was evident with 98% of caregivers rating it as important for the measure of HRQoL. Inclusion of this dimension on a new measure would be imperative.

The importance of the WSU dimension became evident in children over the age of one year. This could be attributed to the fact that children under one year of age were thought, by some caregivers, to be too young to feel WSU. Furthermore if these constructs were experienced by the child it was thought to affect the caregiver more than the child. It was further difficult for caregivers to score the dimension of WSU in children under one year with reasons given for experiencing problems with WSU including hunger, guessing and a lack of facial expression. After the age of one the importance of WSU increased as caregivers reported a more visible link between the child's emotions and their ability to play, learn and develop. Thus

if there was any change in play, learning or development it would indicate a problem or conversely if there was no change it excluded WSU.

Caregivers discussed relationships between dimensions such as the ability to move, play and wash and dress for older children. This was not as clear for younger children and would need to be explored further with experts in the field. Relationships between dimensions could have the potential of collapsing two items into one larger dimension.

4.6.4 Items which Could be Added

The highest number of suggested items was in the younger age groups, most notably the 0-1 year group. Communication and eating were identified additional items which were of importance across all of the age groups. Communication was seen as important for a number of caregivers as they felt that if their child was not physically able to participate or complete a task they were able to do this through communication with their family or peers. Eating was seen as a fundamental attribute for health. Sleeping was suggested as a new item for children in the age band 0-3 years as caregivers felt that if children were unable to sleep well it would reduce their ability to play or learn. Potty training emerged as a new item for the age band of 1-6 years. The other suggestions related to existing dimensions but with change in nomenclature. Movement, as opposed to walking about, was suggested for the age group of 0-1 years. Play as an item on its own, as opposed to a list of descriptors under UA, was suggested across age groups as the descriptors of hobbies, sports and going to school were not deemed appropriate for younger children. Walking was suggested as an item due to the poor understanding of the term 'walking about'. Discomfort and worried were suggested to be added as separate items. The dimension of SC was suggested to be re-worded as assistance with self-care.

4.6.5 Framing of Questions and Layout

Comparison of child's behaviour 'today' to the child's normal behaviour was associated with condition groups. Most TD children's behaviour 'today' being compared to that of other children whereas, most of the CI children's behaviour 'today' was compared to their normal behaviour. Comparing the skills of the child to other children of the same age needs to be considered as 48% of all caregivers compared their children to others when completing the Mob dimension. This was higher in the 0-3 year age category where 53% of caregivers compared their children to others when answering the Mob dimension. Similarly, when completing the dimension of UA caregivers considered the behaviour of other children in 42% of the cases. This was similar across all of the age groups. Descriptors of SC tasks would need to be considered as

only 39% of caregivers considered the behaviour of other children when completing the question. The three dimensions of Mob, UA and SC are considered more observable and are thus referenced to others easier. The comparison to the behaviour of other children is of importance as it improves the observability of the behaviour and could thus translate into improved objectivity with proxy completion if included in a new measure. PD and WSU were compared to the child's own behaviour 96% and 87% respectively rather than that of other children. Caregivers have 'normed' their child's behaviour although there is no 'norm' for emotion. Furthermore, there was no association between the age of the child and comparison to the child's behaviour or their normal behaviour for both PD and WSU. These two dimensions are less observable and thus comparison to other children is more challenging.

The suggested changes to wording included changing 'walking about' to refer only to walking, or in the case of younger children to movement. The dimension of SC was suggested as being changed to 'assisting with washing and dressing'. The descriptors given under UA were thought to be mostly inappropriate and the suggestion was to change the item to play with no other qualifiers of UA. Although the PD dimension performed well across age groups and condition groups it was suggested that the word discomfort be removed. Similarly the three descriptors for WSU were problematic with many suggestions for only keeping one or two of the three descriptors. The levels of report and instructions were well understood and accepted by caregivers.

The rating of general health on the VAS was difficult for a number of caregivers to understand. There was uncertainty as to what the term 'health' encompassed. This led to the suggestions that an explanation of health was included as well as explanations for the terms of best and worst health. Other suggestions included adding descriptions, scenarios or pictures to the anchors of 'best health' and 'worst health'. The number of caregivers with suggested layout and wording changes to the VAS were very small. Across the sample VAS scores performed as predicted across AI, CI and TD children suggesting that comprehension was generally good.

4.6.6 Study Limitations

The study was limited to a small group of the population as only English speaking individuals were included. The majority of the families utilising the acute and chronic care facilities were Afrikaans and Xhosa speaking and were thus not eligible to participate. The recruitment process of caregivers of TD children was also biased toward the middle class community as a pre-requisite to attending the day-care centre was to be an employee of the children's hospital. By the nature of the work at the children's hospital most of the caregivers had accessed higher education and had a better understanding of health. The cognitive

interviews were time consuming and had a high cognitive burden on the respondents which may have compromised the richness of the data.

A further limitation of the study included the condition groups (AI, CI and TD) in which the children were categorized. The chronicity of their child's health condition could have affected the caregivers understanding of health terms and their acceptance or adaptation to having an ill child. The study design did not allow for in depth analysis of the severity or chronicity of the child's health condition.

4.7 Conclusion

There is an identified need for measuring the HRQoL in children aged 0-3 years. But consideration needs to be given to the criticism from the mapping literature review (Chapter 3) and from the caregivers on the current dimensions and developmental process of the EQ-5D-Y. Criticism from the literature review includes the fact that it was not developed with a clear conceptual framework, the dimensions are not all observable, and there is ambiguity in some of the dimensions with reference to more than one construct as with worried, sad or unhappy. This is essential in ensuring accurate measure of HRQoL in this vulnerable age group. There is a need to identify a definition and framework from which to develop a measure for very young children. The adapted ICF model identified in the narrative review (Chapter 2) would be recommended for the basis of a new measure. The dimensions included in the EQ-5D-Y proxy are important in childhood but as currently phrased they are more relevant for older children (3-7 years). Thus, additional dimensions and dimension descriptors need to be adapted to be more appropriate for the very young child. The developmental progression may account for the fact that the dimensions are not significant between AI, CI and TD children under three years of age. The FDA suggest that proxy measures should be based on observable dimensions – the results suggest that the dimensions of Mob and UA are more observable with comparison to other children but SC; PD and WSU are less observable and compared to the child's normal behaviour. Play was considered the most important function of children and similarly to the other descriptors of UA the achievement of this was dependent on environmental factors. Although there were suggested layout changes, these were few in number and those suggested would substantially alter the structure of the EQ-5D-Y which was found to be favourable for the development of a preference based measure.

The importance of dimensions and suggestion of new dimensions needs to be re-evaluated together with a panel of experts in child health, child development and HRQoL experts. Candidate items identified through the literature reviews and cognitive interviews will need further testing by experts in the panel to assess

their relevance. The applicability of dimensions and the performance thereof will become more apparent with further development and testing of the measure.

5 Chapter 5: Reduction of the Item Pool and Descriptor Development with an Expert Panel

5.1 Introduction and Background

Results from the mapping literature review (Chapter 3) identified that there was the biggest need to develop a new HRQoL measure for children aged 0-3 years. These results were further strengthened by the results from the cognitive interviews and testing of the EQ-5D-Y Proxy which indicated that the EQ-5D-Y Proxy did perform well in children aged 4-7 years but the dimensions needed revision in children aged 0 – 3 years. Dimensions, as currently developed on EQ-5D-Y Proxy, performed poorly in cognitive interviews in this very young age group and revision of the dimensions needed to be considered. It was thus concluded that the process of developing this new instrument should proceed and the next step was to identify a definitive set of items reflecting the most important dimensions in this age group. The development of the item bank in this study followed a similar procedure to that described for measures identified in the mapping review (Chapter 3). The candidate item bank includes items identified in the literature review, cognitive interviews with caregivers of the target population and expert opinion in the form of a workshop. The list of candidate items was then further refined in line with the ICF used as a conceptual framework and the reduction of items was then done by a Delphi panel of experts. This chapter describes the process of item reduction through the Delphi panel.

There were other issues that needed consideration by the Delphi panel. The workshop with experts in the field debated possible age cut-off points for different instruments. The age range for inclusion could be based on normal age-related neurological development. If the normal variation in development of gross motor tasks such as walking is taken into consideration the age range for inclusion would be suggested as 0-2 years. However, if one accounts for the normal variation in development of communication and social interaction the age range for inclusion should be considered as 0-3 years [86]. It was then suggested that children over three years of age typically have the ability to self-report, an instrument developed for this age group (4-7 years) could rely on self-report rather than proxy report. The Delphi panel was thus asked to reach consensus on the age cut-off point for the mooted new instrument. There was debate about the appropriate use of descriptors in a potential new measure to ensure the observability of the dimension [86]. This was a further matter which we hoped to address through the two part Delphi study.

The top ranked candidate items identified through this Delphi study would be included for further testing and reduction in an Alpha Draft of the new measure.

5.2 Aim and Objectives

The aim of this section was to generate an appropriate item pool for the Alpha version of the HRQoL measure for children. The specific objectives of the study included advising on the target age range of the new instrument and identifying a smaller number of items which were deemed developmentally appropriate, observable and appropriate for proxy report for the age range of inclusion. A further objective was to identify appropriate descriptors for the items taking into account the developmental trajectory of the target group.

5.3 Methodology

A quantitative, consensus study was done with data collected by means of an e-mail co-ordinated Delphi technique using the Content Validity Index (CVI).

5.3.1 Participants

Purposive sampling was used and experts were selected on their knowledge of both HRQoL and child health. The 15 selected participants included international experts in HRQoL, child health and child advocacy. Participants were invited to participate in the study via e-mail invitation.

The sample was selected based on the group of experts that were known to the research group. The decision was made not to include caregivers in this group of experts as their views would be heard during the cognitive interviews. Professionals who practiced within a multi-disciplinary team and who had a vested interest in HRQoL and/or Health Economics and/or child development or who were active advocates for child health were included in the study. Researchers with a background in EQ-5D-Y were included as they were thought to have in depth knowledge of the performance and challenges with the current instrument. Although they may have been biased toward the existing items on the EQ-5D-Y, this was thought to be less of a problem as they would form part of a group of professionals and inclusion of items would ultimately need justification by participants. Every effort was made to include experts from a range of institutions and backgrounds. This was however limited due to the contacts within the research group.

5.3.2 Instrumentation

The design of the Delphi Questionnaire was based on templates which were available in the Survey Monkey survey management programme. Participants were asked to rate a list of items (those generated from reviews of the literature and cognitive interviews with the caregivers) on a CVI from 1-4 (Appendix 9) for each of the age groups. The age of inclusion in the age groups was from birth – 11 months 30 days (0-12 months), 12 months 0 days – 23 months 30 days (12-24 months) and 24 months 0 days to 35 months 30 days (24-36 months). The CVI ratings scale from 1-4 were characterised as 1- not relevant, 2- somewhat relevant, 3- quite relevant, and 4- highly relevant. The participants were then asked to suggest any new items which they felt needed to be added to the item pool. Participants were also asked to select the number of items which should ideally be included in the new questionnaire as well as the age-range of children which should be included. The questionnaire was pre-tested by two independent researchers to approve the content, structure and comprehension of questions. Necessary changes were made according to their input.

Candidate items to be tested in round one of the Delphi study are shown in Table 5-1 and are based on the candidate items arising out of the literature review and the cognitive debriefing exercise. They were arranged alphabetically to decrease potential bias. Due to the burden on the participants we had to rationalize the inclusion of items which were very similar. The participants were given the opportunity in the second round to suggest new labels for the items.

Table 5-1 Candidate Items

Review of Generic HRQoL measures	Cognitive interviews	Delphi Study Round 1
Walking/Ambulation	Walking	Walking
Mobility	Movement	Movement
Physical function		
	Upper Limb Movement	Upper Limb Movement
	Kicking	Kicking
	Crawling	
	Achievement of Milestones	Achievement of Milestones
Family Activities		
Family Cohesion		
Social		
Relationships		Relationships
Doing things with family or friends	Socializing	Socializing
Usual Activities	Usual Activities	Usual Activities
Washing	Washing	Washing
Dressing	Dressing	Dressing
Hobbies	Hobbies	Hobbies
Sport		
Playing	Playing	Playing
School	School	Pre-School
	Learning	Learning
	School Performance	
Cognition	Cognition	Cognition
	Perception	
Mental Health		
	Motivation	Motivation
	Attitude	
Emotion	Emotion	Emotion
Behaviour		Behaviour
Worried	Worried	Worried
Sad	Sad	Sad
Unhappy	Unhappy	Unhappy
	Routine	Routine
Self-care		Self-care
Independence	Independence	Independence
	Dependence on Care	Dependence on Care
Sleeping	Sleeping	Sleeping
Eating	Eating	Eating (able to take food orally)
	Feeding	Feeding (Ability of child to feed him/herself)
	Growth	Growth
Toileting	Toileting	Toileting
Pain	Pain	Pain
Discomfort	Discomfort	Discomfort
Mood		Mood
Energy		Energy
Self-Esteem	Self-Esteem	
General Health		
	TB Status	
	HIV Status	
	Sickness	Sickness
	Immunizations	Immunizations
Dexterity	Dexterity	Dexterity
Senses	Senses	Senses
Communication	Communication	Communication
Environment	Supportive Environment	
Religion	Spirituality	Religion
	Trust	
	Attitude	
	Hygiene	Hygiene
	Pride	Pride
	Burden of Care	
	Following Rules	

Items highlighted in grey were not in keeping with the definition of HRQoL and were thus excluded.

The second Delphi questionnaire was based on the results obtained from the first round. The aim of this round was to reach consensus on a smaller list of items to be considered for each age group as well as the importance of each item and suggestions for items descriptors. Participants were thus asked to rank the items according to importance for each of the age groups. Thereafter they were asked to give a reason for inclusion of the ranked item as well as a suggested descriptor for each of the items. Their suggestion for items which could be combined as one item was also sought. This process ensured that similar items were not chosen which represented the same item but worded differently. Furthermore the list of items could be further condensed when two items were thought to be equivalent. The second Delphi questionnaire was also piloted by two independent researchers to ensure content, structure and comprehensibility of the questions was appropriate.

5.3.3 Procedure

Ethical approval was obtained from the UCT HREC (HREC/REF: 336/2014) (Appendix 2). International experts were selected based on their perceived knowledge of HRQoL and/or Health Economics and/or child development. Participants were invited to participate in the item pool generation via e-mail. As not all participants were experts in HRQoL the e-mail included an explanation of HRQoL, HRQoL dimensions according to the EQ-5D-Y Proxy and the study and a link to the online survey management system of Survey Monkey. All information was gathered from participants using Survey Monkey software. Willing participants were asked to give informed consent and agree to participate in the process within a three week time period. All participants who had not participated in the Delphi survey were sent a reminder after two and a half weeks. After informed consent (Appendix 8) was obtained, participants were asked to rate the item on a CVI from 1-4 (Appendix 9) (1- not relevant, 2- somewhat relevant, 3- quite relevant, 4- highly relevant). The participants were given an opportunity to suggest new items to be added to the item pool. Participants were also asked to give their opinion on number of items to include in the questionnaire. The first round of the Delphi study took approximately 20 minutes. Participants were blinded to each other. The participants were allocated a number for summary reports as well as data analysis to ensure confidentiality. The researcher collated the information received.

The participants who completed the first round of the study were invited to participate in the second round of the study. They were asked to complete the second round within a three week period. All participants who had not participated in the second Delphi survey were sent a reminder after two and a half weeks. The second round of the survey included the items with a CVI≥0.75, from the first round of the study, for each age group. Participants were asked to rank the top seven items for each age group (a value of one reflecting the most important item). Participants were asked to give reasoning behind selecting each of the

top ranked items as well as suggestions for descriptors. Participants were also given the opportunity to identify items which could be combined under a different title as well as suggesting any items which they felt should have been included. The second round of the Delphi study took approximately 25 minutes. Participants were blinded to each other. The participants were allocated a number for summary reports as well as data analysis to ensure confidentiality. The facilitator of the Study, JV, collated the information received.

The results were analysed and a summary report was sent to all participants with the final item selection. The identified items were incorporated into the Alpha version of the questionnaire for further testing.

5.3.4 Data Management

The information given by each participant was captured by Survey Monkey, a secure online survey management tool. The account was password protected and accessible to the researcher only. The information from the Delphi study was entered into an Excel spread sheet. The information was saved on a secure, password protected e-mail account. The participants had access to a summary report of the Delphi study. The researcher and the research supervisors had access to the raw data as well as the analysed data.

5.3.5 Statistical Methods

Statistical analysis was conducted using Microsoft Excel. The Delphi study was an important step in ensuring the content validity of the instrument thus the scoring system of the CVI which was used successfully by other instrument developers was selected [249]. The CVI from round one for each item was computed on the CVI template (Appendix 9) and was the number of experts giving a rating of either three or four divided by the total number of experts as suggested by Polit and Beck (2006) [249]. The cut-off point of inclusion of an item was taken from Polit and Beck (2006) with a recommendation of a CVI of ≥0.78 for 6-10 participants. As there were 12 participants who completed the first round of the Delphi study a score of 0.78 was not possible thus the accepted score was changed to ≥0.75. The ordinal scale was dichotomized into relevant and not relevant based on a cut-off point of CVI of ≥0.75 [249].

Additional participants were not recruited to take part in the second round of the Delphi study as the aim was to reach consensus amongst the same group of participants. Literature further indicates that a minimum of three experts is needed to draw conclusions regarding content validity [249]. The items used in the second round of the Delphi study were as a result of the rating exercises of the participants in the first round. As is the nature with a Delphi study other participants may not have reached the same results and

thus it may have been confounding for them to participate from the second round. Due to the smaller than anticipated number of participants in the second round of the study the CVI score as well as a weighted average score was obtained. This was to ensure that there was no bias introduced due to the CVI method selected for the larger number of participants. The weighted average was calculated with the first ranked item scoring seven points and the seventh ranked item scoring one point for each participant. These weighted average scores were then combined to calculate a weighted total score. These items were not included based on a certain cut-off value but rather the top scoring items from each method were examined. The top ten items had a CVI total score of ≥0.63 which was considered to be acceptable for the small number of participants. The other items all scored substantially lower. The weighted total score was compared to a CVI total score (calculated by the sum of CVI scores for each age group).These scores were compared and no difference was found for the top scoring items for either method. The top ranked items were incorporated into the Alpha measure for further testing.

5.3.6 Ethical Consideration

Ethical principles of autonomy, confidentiality, beneficence/non-maleficence and justice applied in the Delphi Study are detailed below and were based on the Helsinki Declaration [243]. The principle of autonomy ensures that the participants' in the study are provided with all of the necessary information so that they are able to pass their own judgements. This includes maintaining the participants' confidentiality and privacy throughout the study. Beneficence/non-maleficence ensures that engagements are to the participants'' benefit and that all potential harm is removed. Justice ensures that the burden or benefits of participating in the study is distributed equally among all potential participants'.

Autonomy

All of the participants who were identified as experts in the field were e-mailed information regarding the study. The e-mail included an explanation of HRQoL, HRQoL dimensions according to the EQ-5D-Y Proxy, detail the purpose of the study, their role in the study, the risks and benefits, the confidentiality of their information and their right to refuse to partake in the study or withdraw at any point. The e-mail included a link to the online survey management system of Survey Monkey where informed consent was taken (Appendix 8).

Confidentiality

The confidentiality of each participant was maintained by keeping the information on Survey Monkey, a secure, password protected internet survey tool. The electronic Excel files were password protected on a

secure computer. Participants were not known to each other and they were not identified in the analysis or write-up of the research.

Beneficence and non-maleficence

The participants did not incur any costs for their involvement in the study and thus no monetary re-imbursement was given. The research had a potential to develop a new HRQoL measure, for very young children, which would be valid and reliable for use in children in South Africa. This would have had future benefit in measuring the HRQoL of very young children. This could have assisted in improved understanding of the child's health condition and could improve management thereof.

There were no known risks to the participants and therefore no insurance was required for research-related injuries. There were no consequences for the three researchers who did not participate in the first round of the Delphi study. There were further no consequences for the four participants who did not participate in the second round of the study.

Justice

As expert opinion was sought participants were selected by the research team according to their perceived knowledge on HRQoL, child health and child advocacy.

5.4 Results Delphi Study Round One

Local and international experts in the field were invited to participate in the Delphi Study. Out of the 15 experts who were invited to participate 12 gave informed consent and completed the online survey. Ten of the participants were female and two were male. Two of the experts were European and the remaining ten experts were from different parts of South Africa. The experts professions included: HRQoL expert and health economist; HRQoL expert with experience developing the EQ-5D-Y; paediatric physiotherapist, researcher at the School of Child and Adolescent Health (UCT); paediatric neurologist, paediatric developmental neurologist, general paediatrician, paediatric psychologist, professional paediatric nurse, paediatric intensivist and a paediatrician with a special interest in pain and palliative care, paediatric rheumatologist who participates in health economic decision making and assists in managing the orphan drug list in South Africa.

There were 42 items to rate for each of the three age groups respectively. The results are for each item and age group are depicted in Table 26. Of the 42 items evaluated for children aged 0-12 months, 31 were did not meet the criterion and the resultant item bank consisted of 11 items for this age group. Of the 42

items evaluated for children aged 12-24 months, 20 items did not meet the criterion and the resultant item bank consisted of 22 items. The first round of the Delphi study resulted in 18 of the items in the initial item bank of 42 to be eliminated. Thus 24 items were considered for inclusion for the age group 24-36 months. Items highlighted in grey scored a CVI>0.75 for children aged 0-12, 12-24 and 24-36 months. Items highlighted in purple scored a CVI>0.75 for children aged 12-24 and 24-36 months (Table 5-2).

Table 5-2 Items with a CVI≥0.75 for the Different Age Groups

0-12 Months	CVI	12-24 Months	CVI	24-36 Months	CVI
		Achievement of Milestones	0.92	Achievement of Milestones	1
		Behaviour	0.75	Behaviour	0.83
				Cognition	0.75
		Communication	1	Communication	1
		Discomfort	0.92	Discomfort	0.92
Eating (Able to take food orally)	0.75	Eating (Able to take food orally)	0.83	Eating (Able to take food orally)	0.92
		Energy	0.75	Energy	0.83
				Feeding (Ability of child to feed him/herself)	0.92
		Growth	0.75	Growth	0.75
				Independence	0.75
				Learning	0.92
Mood	0.75	Mood	0.75	Mood	0.92
Movement	0.83	Movement	0.92	Movement	0.83
Pain	0.1	Pain	1	Pain	1
Play	0.83	Play	0.92	Play	0.92
Relationships	0.83	Relationships	0.92	Relationships	0.92
		Routine	0.83	Routine	0.83
		Sad	0.92	Sad	0.92
Senses	0.75	Senses	0.92	Senses	0.75
Sickness	0.92	Sickness	0.92	Sickness	0.92
Sleeping	0.83	Sleeping	0.92	Sleeping	0.92
		Socializing	0.92	Socializing	1
Unhappy	0.83	Unhappy	0.92	Unhappy	0.92
Upper limb Movement	0.75	Upper limb Movement	0.92	Upper limb Movement	0.83
		Usual Activities	0.92	Usual Activities	0.83
		Walking	0.83	Walking	1
				Worry	0.75

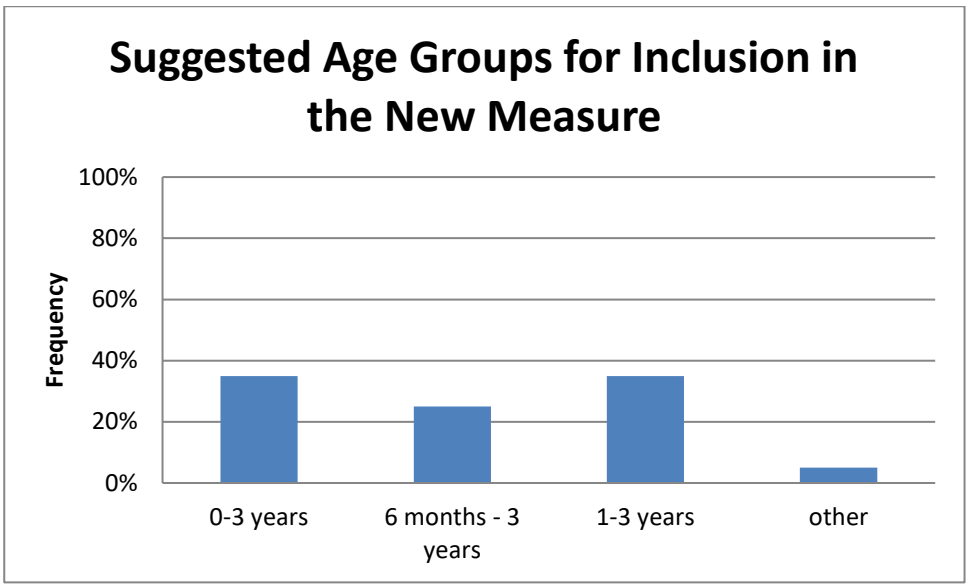


Figure 5-1 Suggested Age Groups for Inclusion in the New Measure

Participant's equally favoured a measure for children aged 0-3 years and 1-3 years for inclusion in the new measure (Figure 5-1).

Table 5-3 Items Distributed for Round 2 of the Delphi Study which included all Items with CVI≥0.75

Dimension	**Items from Delphi Round 1 results**
Physical Functioning	Walking
	Movement
	Upper Limb Movement
	Achievement of Milestones
	Play
	Relationships
	Socializing
	Communication
	Usual Activities
	Feeding (Ability of child to feed him/herself)
	Routine
Cognitive and sensory function	Learning
	Cognition
	Senses
	Independence
Mood	Mood
	Behaviour
	Worried
	Sad
	Unhappy
	Crying
Physiological functions	Sleeping
	Eating (able to take food orally)
	Growth
	Pain
	Discomfort
	Energy
	Sickness

The top 28 scoring items across the age groups from round one are summarised in (Table 5-3) and were further tested and reduced in the second round of the Delphi study. These were roughly grouped into four accepted dimensions of HRQoL to ensure that the spectrum of items was rated in the subsequent round.

Feeding was categorized as a physical function as it was dependent on the child's ability to feed him/herself. Eating was seen as more of a physiological function as it was the ability to take food orally which could be related to oral control, safety of swallowing and the ability of food to pass into the stomach via the oesophagus.

5.5 Results Delphi Study Round Two

The twelve participants who completed the first round of the Delphi Study were invited to participate in the second round of the study. Only eight participants participated in the second round of the study. All eight participants completed the questions regarding the age group 0-12 months. Seven participants completed the questions regarding the age group 12-24 months. Six participants completed the questions regarding the age group 24-36 months. One of the participants sent an e-mail apology for only completing the first section as she ran out of time to complete the survey.

5.5.1 Results for Item Ranking by Importance

Due to the small number of participants in the second round of the study, the weighted average score was calculated in addition to the CVI score as well. This was to ensure that there was no bias introduced due to the CVI method selected for the larger number of participants. The weighted average was calculated with the first ranked item scoring seven points and the seventh ranked item scoring one point for each participant. These weighted average scores were then combined to calculate a weighted total score. Inclusion of these items was not based on a certain cut-off value but rather the top scoring items from each method were examined. The top ten items had a CVI total score of ≥0.63 which was considered to be acceptable for the six participants who completed the entire survey. The other items all scored substantially lower. The weighted total score was compared to a CVI total score (calculated by the sum of CVI scores for each age group).These scores were compared and no difference was found for the top scoring items for either method. The top ranked items were incorporated into the Alpha measure for further testing. These CVI scores were not based on guidelines in the literature but rather by examining the top scoring items for each of the statistical methods employed.

Table 5-4 Weighted Score and CVI for Items by Age Group

Age Group	Ranked Position							Weighted	CVI
0-12 months	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**Total**	**(n=8)**
Eating (Able to take food orally)	28	6	0	0	3	2	0	39	88
Pain	14	0	5	4	3	0	1	27	75
Play	0	6	10	8	0	0	1	25	75
Sleeping	0	6	5	8	3	2	0	24	75
Relationships	7	6	5	0	0	2	0	20	75
Mood	7	6	5	0	0	2	0	20	50
Movement	0	6	0	8	3	0	1	18	63
Crying	0	12	0	0	3	2	0	17	50
Sickness	0	0	5	0	3	4	2	14	75
Senses	0	0	0	0	6	0	2	8	50
Unhappy	0	0	0	1	0	0	1	2	25
Upper limb Movement	0	0	0	0	0	0	0	0	0
12-24 months									**(n=7)**
Play	0	18	10	0	3	0	0	31	76
Eating (Able to take food orally)	21	0	0	0	0	0	0	21	43
Relationships	0	6	5	4	0	0	2	17	71
Sleeping	0	12	0	0	0	4	0	16	57
Pain	14	0	0	0	0	2	0	16	43
Mood	7	6	0	2	0	0	0	15	57
Behaviour	0	0	5	8	0	0	0	13	43
Growth	7	0	0	0	3	2	0	12	43
Communication	0	0	5	0	3	2	0	9	43
Achievement of Milestones	0	0	5	0	0	2	1	8	71
Socializing	0	0	0	4	3	0	0	7	43
Energy	0	0	5	0	0	0	0	5	14
Sickness	0	0	0	0	3	0	1	4	29
Senses	0	0	0	0	3	0	0	3	14
Usual Activities	0	0	0	0	3	0	0	3	14
Walking	0	0	0	0	0	2	0	2	14
Movement	0	0	0	0	0	0	1	1	14
Unhappy	0	0	0	0	0	0	1	1	14
Routine	0	0	0	0	0	0	1	1	14
Upper limb Movement	0	0	0	0	0	0	0	0	0
Discomfort	0	0	0	0	0	0	0	0	0
Sad	0	0	0	0	0	0	0	0	0
24-36 months									**(n=6)**
Play	0	12	5	0	3	0	0	20	67
Mood	14	0	0	0	0	2	0	16	50
Independence	0	0	5	4	0	4	0	13	67
Relationships	7	6	0	0	0	0	0	13	33
Sleeping	0	6	0	4	0	2	0	12	50
Usual Activities	0	6	0	0	3	0	2	11	67
Eating (Able to take food orally)	7	0	0	4	0	0	0	11	33
Behaviour	0	0	5	4	0	0	1	10	50
Routine	7	0	0	0	3	0	0	10	33
Socializing	0	0	5	0	0	4	0	9	50
Walking	7	0	0	0	0	0	0	7	16

Sickness	0	0	0	0	6	0	0	6	33
Growth	0	0	5	0	0	0	0	5	16
Energy	0	0	0	4	0	0	0	4	16
Feeding (Ability of child to feed him/herself)	0	1	1	0	0	0	0	2	33
Learning	0	0	0	1	0	0	1	2	33
Movement	0	0	0	0	1	0	0	1	16
Discomfort	0	0	0	0	0	0	1	1	16
Worry	0	0	0	0	0	0	1	1	16
Senses	0	0	0	0	0	0	0	0	0
Unhappy	0	0	0	0	0	0	0	0	0
Upper limb Movement	0	0	0	0	0	0	0	0	0
Sad	0	0	0	0	0	0	0	0	0
Cognition	0	0	0	0	0	0	0	0	0

1= most and 7 = least important;

- In the 0-12 month category, eating was ranked as the most important item, followed by pain. Apart from mood, the nine top ranked items received a CVI of 63 or above. Sickness had a high CVI but the weighted total was low.
- In the 12-24 month category, play had the highest weighted score, followed by eating and relationships. The top ranked 11 items received a CVI of 43 or higher. Additional items to the younger age group identified for the 12-24 month age group include: mood, behaviour, growth, communication, achievement of milestones and socializing.
- In the 24-36 month category, play and mood were ranked the most highly. In the top ten ranked items, only seven had a CVI of 50 or above and these were considered. Relationships, eating and routine were ranked in the top ten but had low CVI.

Similar items were identified across the age groups. To compare the items which were generated across the age groups, the two different methods of determining item importance need to be combined across the three age groups. The results can be seen in Table 5-4; the weighted total for each item for each age group and the CVI for each age group were added together. The items were then ranked according to the combined score for totals and CVI respectively. As many of the items had similar meanings participants were asked to identify items which they felt could be combined under one label heading and what label that would be. The label would then represent a 'dimension', rather than discrete items, several of which could be included in one dimension. Duplicate suggestions were removed for each age group. Most of the items which were combined formed either a dimension of mobility, emotion or social interaction across all three age groups (Table 5-5). With the advancement of age there appear to be more items which would be grouped together to form one new label. One needs to take these combinations of dimensions into account when selecting items.

Table 5-5 Items to be Combined for Children Aged 0-36 Months into a Suggested Dimension

	Item	**Item**	**Item**	**Item**	**Item**	**Label for Dimension**
0-12 months	Upper limb mvt	Movement	Play			Movement
	Movement	Upper limb mvt				Movement
	Upper limb mvt	Movement	Play			Play
	Crying	Mood	Unhappy			Mood
	Unhappy	Mood				Mood
	Mood	Crying	Pain	Unhappy		Mood
	Relationships	Play				Social Interaction
	Crying	Pain				Pain/discomfort.
						(Crying used as a descriptor to indicate severity)
12-24 Months	Movement	Upper limb mvt	Walking			Movement (with age specific expectations)
	Play	Achievement of milestones	Walking	Usual Activities	Upper limb mvt	Play or movement
	Walking	Achievement of milestones	Movement			Movement
	Walking	Achievement of milestones	Communication	Upper limb mvt		Achievement of Milestones
	Mood	Unhappy	Sad			Positive: Smiling
						Negative: Sadness/crying
	Mood	Unhappy	Sad	Energy		Mood
	Discomfort	Mood	Unhappy			Mood
	Mood	Unhappy	Behaviour	sad		Behaviour
	Relationships	Communication	Socialising			Relationships
	Relationships	Communication	Socialising			Communication
	Social activities	Routine				Routine activities
	Eating	Energy	Growth			Growth
	Pain	Discomfort				Discomfort
	Pain	Sickness	Discomfort			Sickness
24-36 Months	Movement	Upper limb mvt				Movement
	Feeding	Walking	Usual Activities			Usual Activities
	Movement	Upper limb mvt	Play	Usual Activities	Walking	Usual Activities
	Feeding	Walking	Usual Activities	Independence		Independent Activities
	Mood	Unhappy	Worry	Sad	Discomfort	Mood
	Mood	Unhappy	Worry	Sad		Mood
	Relationships	Socialising				Relationships
	Mood	Unhappy	Behaviour	Sad	Worry	Behaviour
	Eating	Growth	Energy	Feeding		Feeding self

Mvt=movement

Finally the items that had the highest mean CVI and highest mean ranking of weighted importance scores for each of the three age groups were identified and presented under the new label (Table 5-6).

Table 5-6 Items with a Significant CVI or Weighted Score for Children Aged 0-36 months.

Top ranked items	**Final label for testing**
Achievement of Milestones	Movement
Movement	
Eating (Able to take food orally)	Eating
Growth	
Play	Play
Usual Activities	
Relationships	Relationships
Socializing	
Behaviour	Behaviour
Communication	Communication
Independence	Independence
Mood	Mood
Pain	Pain
Sleeping	Sleeping
Sickness	Sickness

Results from suggested grouping of items to form new dimensions were considered and the final dimension names to be tested are indicated in the right hand column (Table 5-6). Respondents suggested that the item achievement of milestones (significant for 12-24 month group only) be combined with the item of movement. Similarly, it was suggested that the item of usual activities (significant for 24-36 month group only) be combined with play. Growth (significant for 12-24 month group only) could be combined with eating. Relationships and socializing are interchangeable in this age group and can also be combined. If these groupings are taken into consideration the top thirteen ranked items across the age groups would be considered for inclusion. Thus the item bank of 28 items tested in the second round of the Delphi study across the three age groups were further reduced to 11 items to be included in the Alpha Draft. Sickness was defined by all of the participants as a term to describe the general health of the child or presence or absence of illness. This is similar to the rating of general health from worst health imaginable (0) to best health imaginable (100) on the VAS rating scale on the EQ-5D-Y. Thus, sickness will be measured by the rating of general health on the VAS. Thus, ten of these will be dimensions on the descriptive system of the measure and one (sickness) will be representative on the VAS rating of general health.

5.5.2 Descriptor Suggestions for Top Ranked Items

The respondents had been requested to provide reasons in support of their support for different items and their reasoning and suggested descriptors are presented in Appendix 12. As their suggestions regarding descriptor or labels for each item informed the formulation of the questionnaire, these are presented below in alphabetical order (Table 5-7).

- Inclusion of behaviour was only considered important from 12 – 36 months of age. Behaviour is thought to indicate health, presence of pain and happiness. Another element of behaviour is suggested as appropriate response to people, environment and activities.
- Communication is described in terms of verbal and non-verbal communication. Descriptors include examples of communication as well as the ability to make one's needs known to the family or the world. The descriptors suggested for children under 12 months is focused on some of the elements of communication with reciprocal interaction with individuals and the child's subsequent enjoyment thereof. Recognition and response to the caregiver is also essential at this age. After 12 months the ability to (verbally) communicate needs to their carer becomes important. There is also an emergence of interaction with other children (socialising) but the emphasis still remains on good interaction with family. After 24 months interaction with other children emerges to a stronger degree.
- Descriptors for eating vary across the age group with the older age group again having a focus on independent feeding. Some of the descriptors suggested for the younger age group may however be applicable across the age group to indicate more about the health status of the child together with growth. These include the child's ability to suck or chew and swallow as well as the absence of subsequent, gagging, reflux or aspiration. Another important indicator for health was suggested as the ability to feed comfortably without fatigue or fussiness.
- Independence was only ranked as important for children 24-36 months of age. Most of the examples given for independence include self-care activities as well as becoming independent in a known environment.
- Mood reflects the construct of emotion from the EQ-5D-Y with the importance of the dimension being justified in terms of happiness or unhappiness, sadness and crying. These traits are classified on other HRQoL measures as emotions (Chapter 3). There is an element of consolability to these emotions or moods with regards to a child becoming irritable when tired or hungry, and judgement would need to be made when not irritable for these reasons. Mood or emotions seems to further form the basis of interaction with both the caregiver and the environment. Behaviours of crying and smiling are suggested to be good descriptors for this dimension.
- The movement descriptors suggest free, smooth and functional movement of all four of the limbs. They are however age specific suggestions with specific limb movements or higher functioning movement for older children such as running and use of hands.
- Pain as a construct is very important in determining HRQoL. Pain is non-specific in younger children and one relies on the caregiver to determine whether the child is expressing distress due to pain or other issues such as hunger or tiredness. Pain can be judged in a child by the persistence of their crying, their interaction with the environment, facial grimacing or general discomfort. In the verbal child, it is often easier to establish the presence of pain. Pain is also said to have emotional and physiological effects. Sickness is considered as a general descriptor for anything which may affect the health of a child.

- It is evident that the repertoire of skills for play is directly dependent on age and the achievement of gross and fine motor skills as well as interaction with others. The interaction with others for play progresses from the caregiver initiating play in the youngest age group, to playing alongside other children for children aged 12-24 months to interactive play for children 24-36 months. Play is however described as being enjoyable and mostly involving objects or toys.
- Descriptors of sleep include the ability to fall asleep, the quality and duration of sleep according to age appropriate requirements.
- Sickness is considered as a general descriptor for anything which may affect the health of a child. Thus sickness, regardless of magnitude, would in effect negatively affect the child's overall HRQoL.

Table 5-7 Summary of the Importance of Dimensions and Suggested Descriptors per Age Group

Dimension	**Age**	**Suggested Descriptor**
Behaviour	12-24 months	• Behaviour appropriate to age. • Response to other people, environment and activities.
	24-36 months	• Behaviour appropriate to age.
Communication	12-24 months	• Able to use the body for communication (hugs, kisses, smiles, crying etc.) • Making needs known. • With family and the world.
Eating	0-12 months	• 0-6 months: will and ability to suck milk. 6-12 months: curious toward food and able to take and taste pieces of food. • Able to suck and swallow/chew and swallow (age dependent) without reflux/aspiration. In older infants - able to finger feed solids and semi-solids. A negative score might provide the option of 'gags when food is placed in mouth'. • Able to feed comfortably without fatigue or fussiness. • Sustaining good nutritional intake, able to swallow well, starting to chew on food appropriately for age. • Able to take food orally. • Feeding related to age.
	12-24 months	• Will and ability to eat autonomously, with cutlery (even if not used correctly) or with hands. • Able to finger feed a variety of foods and textures. • Growth and general well-being. • Putting on weight and increasing in height. • On normal growth parameters.
	24-36 months	• Able to feed themselves using at least a spoon, enjoying food and no difficulty with swallowing or retaining food. • Eat independently. • Parameter of growth chart.
Independence	24-36 months	• Able to eat independently; able to dress independently; able to go to the toilet independently; able to wash face independently. • Self-care activities. • Able to wash and dry hands, brush teeth with help and put on a T shirt. • Able to be left with carer.

Mood	0-12 months	• Draws attention. • Mood items might have options of: 'mostly content', 'cries occasionally' and 'cries often'. • Generally content, may be irritable when tired or hungry. • Generally cheerful and responsive, rarely irritable, no major fluctuations in mood.
	12-24 months	• Being in a negative mood frequently. • Mostly content/happy; cries occasionally; cries often; inconsolable. • Generally content, expresses frustration and displeasure appropriately. • Mood stable, and generally content.
	24-36 months	• Mostly content; unhappy some of the time; unhappy most of the time; inconsolable. • Generally content. • Cheerful and energetic with no inappropriate swings in mood.
Movement	0-12 months	• 0-6 months: able to move arms and hands and legs and feet, and head, eyes, specific according to his age. 6-12 months: able to use arms and legs and head to explore, move from one place to another, to play with small object/toys. • Able to run around. • Movements smooth and functional. • Moving freely in age-appropriate fashion. Able to move all limbs without constraints. Using hands well. • Moving all four limbs freely.
	12-24 months	• Able to move generally and freely without discomfort. Able to move and use hands particularly • Able to move freely, and without pain or discomfort; particularly moving hands and upper limbs well.
	24-36 months	• No suggestion.
Pain	0-12 months	• 0-6 months: continuous and/or anomalous pain - e.g. colic is normal. 6-12 months: anomalous pain - e.g. pain to foot/hand or other parts of the body. • Having pain or discomfort. • Consider scale of 'always', 'often', 'occasionally' or 'never' in pain. • Daily activities not hampered by persistent or severe pain.
	12-24 months	• Complaining of any pain. • In pain all of the time, most of the time; some of the time; never.
	24-36 months	• Pain/ discomfort.
Play	0-12 months	• 0-6 months: able to follow objects, things/persons moving around then able to take/touch objects with hands/feet. 6-12 months: able to use objects to see what happens -throwing a ball, playing with food. • Able to play. • Able to engage in age-appropriate play (with examples for each age group). • Playing with toys, and starting to interact with other infants and children. • Engaging in an enjoyable activity.
	12-24 months	• Will to play (explore) with anything. • Able to engage in play behaviours (not necessarily through limb movement). • Able to play alongside other children, engages in one on one activity with caregiver. • Playing with other children, playing with toys and any objects in environment. • Engaging in a specific activity for enjoyment.
	24 -36 months	• Able to play physically/cognitively at an age/condition appropriate level. • Imaginative play by alone and with others, takes turns. • Playing normally with other children and with the toys. • Using physical abilities, problem solving skills and language to engage joyfully with other children. • Walk up and down stairs without, jump, throw a ball, stack 6 blocks, draws a vertical line. • Pertaining to some independence.

Relationships	0-12 months	• Recognises and responds positively to mother/significant carer. • Able to interact and form relationships with significant others. • Making eye contact well, responding appropriately to speech, recognising individuals and family members and enjoying social contact.
	12 -24 months	• Able to communicate basic needs to carers. Able to play/socialise with other children of similar ages. Displays a strong bond with carer. • Recognises and responds with affection to family and close friends. • Recognises people, interacts well with family and close friends. • Knows family and recognises a stranger. • Developing a sense of self in relation to other people. • Acting appropriately with other people.
	24-36 months	• Strong bonds with family and close friends. • Relating well to family, friends and peers and communicating well. Able to communicate at an age- and condition appropriate level with other children and carer/s. • Ability to play and interact with others. • Able to engage with other children.
Sickness	0-12 months	• 0-6 months: sickness identified according to complaints of the mother. 6-12 months: sickness identified according to complaints of the child. • Having health impairments. • Generally healthy apart from occasional minor illnesses. • Unwell with temperature or vomiting or continuous crying or diarrhoea or lethargy. • Can compromise development.
	12 – 24 months	• Having a mild (e.g. Flu) or severe (e.g., gastroenteritis, allergy, cancer) sickness. • Generally well apart from occasional minor childhood illnesses.
Sleeping	0-12 months	• This would be age-dependent, could categorise into number of hours continuous sleep per night/number of awakenings? Or good QOL might require - falls asleep easily and generally sleeps well. • Has a regular sleep pattern that is age appropriate. • Regular uninterrupted sleep without disturbances and nightmares. • Eyes closed and body still for an hour or more.
	12 – 24 months	• Able to fall asleep easily and stay asleep for most of the night. • Has regular sleep times during the day, sleeps well at night. • Sleeps well without disturbance; normal sleep patterns; no abnormal waking or bad nightmares. • Sleeps through the night.
	24-36 months	• Good sleep patterns without regular waking at night. • Enough for age to maintain healthy body and mind.

The candidate dimensions were then mapped to ICF categories to examine whether the proposed instrument would reflect the conceptual framework identified in 2.3.4.2. Table 5-8 below lists the top eleven ranked items (after combining items into a new dimension) and their respective International Classification of Functioning and Disability – Child and Youth (ICF-CY) category, descriptor and code. As per the recommendation by Cieza et al (2002), who maintains that the mapping to ICF components may be useful to explore content validity and can facilitate the comparison of HRQoL instruments, the items were mapped to the ICF components to establish if each component was represented in the new measure [104].

Table 5-8 Final Dimensions for the Alpha Questionnaire Classified According to the ICF-CY Categories

	Dimensions	**ICF Category**	**ICF Descriptor**	**ICF Code**
1	Behaviour	Body Structure and Function	Higher-level cognitive function Dispositions and intra-personal functions	B164 B125
		Activities and Participation	Complex interpersonal interactions	D720
		Environmental Factors	Individual attitudes of immediate family members	E410
2	Communication	Activities and Participation	Speaking Pre-talking	D330 D331
3	Eating	Activities and Participation	Self-care – activity of eating	D550
		Body Structure and Function	Sensations associated with the digestive system Ingestion Functions	B535 B510
4	Independence	Activities and Participation	Undertaking single task Understanding multiple tasks Acquiring Skills	D1021 D220 D155
5	Mood	Body Structure and Function	Physical stability Emotional Function	B1263 B152
6	Movement	Body Structure and Function	Neuro-musculoskeletal and movement-related function	B7
7	Pain	Body Structure and Function	Sensory Function and Pain Sensation of Pain	B2 B280
8	Play	Activities and Participation	Learning through actions with objects Acquiring skills Informal social relationships Recreation and leisure Engagement in Play Play	D131 D155 D750 D920 D880 D9200
9	Relationships	Activities and Participation	Basic interpersonal interaction Forming Relationships Family Relationships Child-Parent Relationship	D710 D7200 D760 D7601
10	Sickness	Activities and Participation	Maintaining one's health	D5702
11	Sleeping	Body Structure and Function	Global Mental Function – Sleeping function	B134

5.5.3 Reference to the Literature for the Dimensions Selected From the Delphi Study

5.5.3.1 Behaviour

The dimension of behaviour is included in three of the fifteen generic HRQoL measures for children under seven years of age (Chapter 3). Behaviour scored significantly for children aged 12-36 months in the Delphi Study. The panel of experts suggest that it behaviour indicates health, presence of pain and happiness. The descriptors proposed by the experts were minimal and included the response to other people, environment and activities. It was further recommended that descriptors of behaviour include age appropriate examples.

The ICF-CY categorizes behaviour into Body Structure and Function, Activity and Participation and Environmental Factors [105]. Behaviour is classified as a body function as it forms part of higher-level cognitive function which is said to be an executive function dependent on the frontal lobes of the brain to regulate appropriate behaviour [105]. It is also classified as a complex interpersonal interaction which requires one to manage these interactions in an appropriate manner which is socially acceptable. The attitudes of immediate family members is classified as an environmental factor which affects behaviour [105].

The complexity of behaviour is supported by research. Research into the behaviour and temperament of children can be traced back to the early 1980s with the development of the Infant Behaviour Questionnaire (IBQ) for children aged 3-12 months [250]. Rothbart (1981), described temperament as individual differences in reactivity and self-regulation [250]. The development of the reliable and valid IBQ was based on parent report of extensive observations of their child in the home situation which would include interaction between the infant and caregiver. The IBQ consists of six dimensions namely: activity level, smiling and laughter, fear, distress to limitations, soothability and duration of orientating. Activity level is scored according to the infant's gross motor movement appropriate for 3-12 months. Smiling and laughter is scored for any situation and fear is categorized by distress to new or intense stimuli. Distress to limitations is defined as the child's reaction of distress if: hungry or refusing food: in a restricted place; being dressed or not being allowed an object of interest to them. Soothability is noted as the child calming to the caregiver or soothing strategies. Duration of orienting is measured by the child's interaction (visual, vocal or tactile) with an object with no change in the environment. The parents are requested to rate the frequency of specific behaviours over the past one or two weeks [250].

The IBQ was recently revised in response to advances in understanding temperament. The valid and reliable revised version (IBQ-R) contains the original six scales as well as eight new scales namely: approach, vocal reactivity, high and low intensity pleasure, perceptual sensitivity, sadness, falling reactivity and cuddliness. The items of vocal reactivity, high intensity pleasure, smiling and laughter, activity level and

perceptual sensitivity make up the positive affectivity/urgency which would have similar personality traits of extraversion in an adult. Negative Affectivity which would equate to neuroticism in adult is characterized by sadness, distress to limitations, falling reactivity and fear. Items of duration of orientating, low intensity pleasure, cuddliness and soothability have been shown to link with the adult personality trait of conscientiousness [251].

The IBQ is only valid for children 3-12 months of age, but further research suggested that behaviour can also be stable between the ages of 18- 36 months. Thus the Early Childhood Behaviour Questionnaire (ECBQ) was developed [252]. The ECBQ differs from the IBQ in that their definition of temperament includes motor and sensory systems, emotion and self-regulation. However the items of the two scales are very similar with the ECBQ including: activity level, attention focusing, attentional shifting, cuddliness, discomfort, fear, frustration, high intensity pleasure, impulsivity, inhibitory control, low-intensity pleasure, motor activation, perceptual sensitivity, positive anticipation, sadness, shyness, sociability and soothability [252].

The measure and conceptualization of behaviour in very young children is complex and multi-dimensional. Items on the IBQ and ECQB overlap with items of movement, emotions, pain or discomfort and sociability or relationships. From the cognitive interviews, Delphi study and ICF-CY behaviour is commonly thought of as the response to interactions. This response could further be thought of in terms of individual reactivity and self-regulation when encountering well-known or new environments or people. The suggested descriptor for this dimension: “Aware of different situations and able to respond appropriately to new places and people”. This would suggest that the child is able to react to a change in environment/activity/carer and they are able to respond through self-regulation. The term appropriately was used as every situation would require a different behavioural response. Places and people were used as a reference as these would be common occurrences to most children. The word activity was not used, as suggested to by one of the experts, as it was felt that the exposure to activity may be limited due to cultural or SES.

The performance of a dimension such as behaviour across the age span of 0-36 months is questionable due to the fact that it was only ranked as important in children aged 24-36 months. This is affirmed with the need for two different instruments needed to measure behaviour: IBQ for children 3-12 months and the ECBQ for 18-36 months. These questionnaires further have a gap in measurement from 0-3 months and 12-18 months which are integral ages in the proposed new HRQoL measure. The descriptor has tried to include behaviour which has been suggested from cognitive interviews, expert opinion and research.

5.5.3.2 Communication

Ability to communicate needs was deemed important by many of the caregivers, especially those of chronically-ill children, from the cognitive interviews (Chapter 4). At this young age children are dependent on their caregivers for assistance with activities of daily living as well as seeking medical help. Caregivers expressed that even if children were not able to assist in tasks as they should if they are able to communicate they can direct necessary assistance for the task. These tasks ranged from toileting needs, play activities and pain. Most caregivers would interpret communication as the acquisition of language however, communication involves the activity of conveying information which emerges in the infant with non-verbal cues [115]–[118]. The use of verbal and non-verbal communication was suggested by the panel of experts. The expert suggested that communication would include: smiling, crying, kissing and indicating comfort with a person (Table 10-39). Communication is considered in the ICF category as an activity and participation.

Early in infancy communication is characterised by the ability to express emotions, share attention or eye gaze with caregiver, acquire the attention of a caregiver, rhythms to their vocalisation and intentional touch. These are seen as essential components for the subsequent development of language [115]. These behaviours are reliably observed by 3-4 months of age as infants are able to control their states of arousal [118]. There is evidence to suggest that caregiver interaction and cognitive stimulation, in early infancy and childhood, directly relates to development in all aspects including communication [115], [116]. Cognitive stimulation is suggested as the reciprocal interaction between the caregiver and child with tasks such as reading, playing with toys and verbal interaction [115]. Pragmatics or the way children use language in a social setting is a vital component of language development. The pragmatic skills evolve as children advance in age; this can be seen with communicative intention where a six month old may direct their attention to an object or person, a 12 month old may name the person with who they want to interact (Dada, Mama), their ability to ask questions emerges from 15-18 months and they are verbally able to express their emotions from 30 months [117].

Thus, communication is dependent on a complex interaction between caregiver and child, cognitive stimulation and development and social interaction with others. The non-verbal phase of communication extends from 0-6 months thereafter children still rely on non-verbal communication such as pointing but start to intentionally repeat sounds. Between 12 and 19 months children learn a number of short single words. Between 19 and 24 months their vocabulary expands rapidly and they are able to start making two word sentences. From 25 to 36 months their command of the language improves so that they are now able to communicate in the form of short stories [117].

Although communication was only ranked as important for children 12-24 months of age (Table 10-39), it is apparent from the literature with detailed descriptions of communication it is relevant across the age group of 0-36 months. The suggested descriptor needs to have well-defined communication parameters for each age group. The suggested descriptor for communication: "(0-6 months: cooing, squealing, eye contact, smiling) (7-12 months: 'gaga' uses gestures like pointing) (12-19 months: single words) (19-24 months: puts two words together) (25-36 months: starts telling stories). The descriptor is based on observable behaviour and describes each significant change in communicative ability across the age group.

5.5.3.3 Eating

The results from both the cognitive interviews as well as the Delphi study indicated that the ability to eat was important for growth, development and life. Loss of appetite and the inability to take food orally would be associated with poor health. Caregivers expressed particular distress to their child's inability to eat due to an acute or chronic illness. In infants the importance of breastfeeding was highlighted for its vital role in mother-infant bonding. One of the experts further alluded to the additional sensory benefits of eating semi-solid and solid food. In the toddler the ability to self-feed with either their hands or utensils emerged (Table 10-40). Although this is important for the suggested reasons of developing independence and dexterity, it is not believed to be of paramount importance regarding the consequence for HRQoL.

The ICF-CY describes eating as a function of the body as it is related to consuming and controlling solids or liquids through the mouth into the body which results in a sensory experience in the digestive system [105]. Eating is also seen as an activity or participation as the task of eating involves bringing the food to one's mouth and consuming it in a culturally appropriate way. The act of using utensils or one's hands to cut or break the food as well as bring it to the mouth can be considered as undertaking a single or multiple tasks [105]. However, the ICF-CY does not code for the nutritional benefit of eating [105].

Nutrition is a vital component of child health as their physical, cognitive, and emotional development is dependent of it [5]. Their nutrition depends on the type of foods that are consumed, which change rapidly during the first two years of life [253], [254]. The WHO recommends exclusive breast feeding for the first 6 months of age [255]. However, many mothers choose to introduce breastmilk substitutes for various factors. One such factor has been to ensure longer periods of nocturnal sleep as advocated by peers and not based on empirical evidence [256]. It was postulated that healthy infant's fed breast milk would have an improved HRQoL compared to infant's fed breast milk substitutes. This was attributed to the fact that breast milk substitute leads to harder stools which could lead discomfort from constipation. Furthermore, the immune protection from breast milk substitute is less than from breast milk leading to the increase in illness and infection [257]. However, a Chinese study found few small differences in HRQoL scores between

infants fed breast milk, breast milk substitute or a mix of the two. The breastfed infants showed a higher score for infant temperament and moods and general health perceptions and parent impact-time and parent-impact emotional [257]. This could be attributed to the increased mother-child bonding of breastfeeding and the subsequent improved emotional development from good bonding [258], [259]. Caregivers are encouraged to introduce solid foods at six months or when children show that they are developmentally ready to expand their eating skills[253], [260]. In a study conducted in the United States virtually all of the infants and toddlers younger than 15 months still drank some form of milk in a day. Below 12 months of age this was typically breast milk or breast milk substitute and thereafter there was an increasing consumption of cow's milk. Furthermore, infants and toddlers were eating the same food as the rest of the family [260]. This is within the developmental guideline in that children between the ages of two and five years should start to eat the same food as the rest of the family[261]. Toddlers require more nutrients and energy relative to their bodyweight to sustain their high levels of activity and their rapid growth. As they have small stomachs it is recommended that they have a balanced diet consisting of three meals a day and snacks [261]. Healthy toddlers are able to adjust their appetite within the day to ensure that they consume enough calories for growth [261][262].

Most of the early learning about food and eating takes place within the family or child care setting and is thus shaped by adult caregivers. The learning is dependent on culture and includes behaviours such as eating with or without a utensil, foods that are available, portion sizes, timing or meal routines and the social context of the meals [254]. Healthy infants and toddlers spend 11 ½ hours eating per week[263]. Thus the social context of the mealtime becomes influential on development. Shared family mealtimes are associated with academic performance, language development, physical health, behaviour, amount of sleep and reduced risk for substance abuse later in life [263].

If the physical, social or emotional aspects of eating are disrupted it could lead to a potential feeding problem [264]. Clinical diagnosis of problems with feeding are varied and could include impairment of feeding or eating skills; intolerance to food, food aversion, loss of appetite for a variety of reasons or pathological behaviours during feeding. Health Professionals often overlook the non-physiological attributes of difficulties with feeding. These include environment and parental factors. Problems with feeding are common and affect 25-45% of typically developing children and up to 80% of children with delayed development [264]. Caregivers often seek medical advice as due to concerns related to poor oral intake and problems sustaining growth. The intervention(s) selected should be individually tailored depending on the reason for the feeding problem but both behavioural and biological factors should be considered and addressed by a multi-disciplinary team [264] [265].

Eating is a complex dimension and the subsequent nutrition and growth is paramount to healthy development with regards to physical, cognitive and emotional components. Eating is also dependent on both culture and food security. The cultural aspects of eating are less important as a determinant of HRQoL. Food security would affect the child's growth and development over time. As the HRQoL measure is intended to measure dimensions of health for today only the issue of long term food security will not be addressed. The dimension would rather aim at addressing the physical functions of appetite and eating on the basis of 'today'. Some of the descriptors suggested by the experts for the younger age group of children are applicable to the functions of appetite and eating across the age groups. These include the child's ability to suck or chew and swallow as well as the absence of subsequent, gagging, vomiting, reflux or aspiration. Another important indicator for health was suggested as the ability to feed comfortably without fatigue or fussiness. These however, constitute a list of very technical descriptions which may be difficult for a caregiver to interpret on a short HRQoL measure. The suggested descriptor is thus: "Adequate oral intake to sustain growth." Adequate would thus imply that the child received enough food today to sustain growth. Importantly the food would be taken via an oral route which would imply that the child has relative ability to suck/chew and swallow.

5.5.3.4 Independence

Caregivers highlighted the importance of participation in self-care activities for their child's development of independence during the cognitive interviews. Independence or activities of self-care were included in 8 of the 15 generic HRQoL measures reviewed. Children under three years of age were not expected, by their caregivers, to be able to carry out functions of self-care such as washing and dressing but were starting to assist with the tasks. Another important aspect of self-care, which became evident for children from 18 months of age, was the emergence of toilet training. The participation in dressing and toileting held particular importance for caregivers of children preparing to go to pre-school (Chapter 4). These activities are complex in nature and their emergence will be dependent on caregiver-child relationship, cultural acceptability and cognitive maturity [119], [235]. This is highlighted in the ICF-CY coding of independence as it is thought to emerge due to the acquisition of skills to undertake a single or multiple tasks[105]. Independence was also only thought to be important in the older age group of children (24-36 months) by experts in the field. Most of the examples given for development of independence also included self-care activities such as eating, toileting, washing and drying hands, brushing teeth and assisting with dressing.

The development of independence is generally poorly documented in the literature. It is often an element of psychological development and functioning. According to Ainsworth's attachment theory a secure attachment style between a caregiver and child will foster the child's independence with exploration [119]. A balance between independence and interdependence (with the caregiver) is imperative for normal

psychological function [119]. The development of independence thus relies heavily on the amount of independence the carer allows the child to take on. This would vary across cultures as well as between individual family units.

The development of descriptors for a dimension of independence proves to be very challenging. Most especially as this is really a trait which emerges later in the age group in question. Self-care tasks seem to be synonymous with the development of independence. The use of utensils for eating is far more culturally specific than activities of washing, dressing and toileting [266], [267]. Taking into account the suggestions from the caregivers during the cognitive interviews the descriptor should include assistance with the activities. The dimension name is thus changed to "helping with daily activities" as suggested by both caregivers and experts in the field. The descriptor for the dimension is suggested as: "Age appropriate assistance with washing, dressing and toileting." The variations in washing, dressing and toileting are vast across the age group. Thus the use of the word age appropriate would include the range of ability across the age group. Reference to age appropriate behaviour would increase the observability of the dimension as caregivers would need to reference their child to the same behaviour of children of a similar age. Although the interpretation could be argued to still include subjectivity it is more objective than having no comparison to age appropriateness.

5.5.3.5 Mood or Emotions

One of the striking findings from the cognitive interviews is that caregivers evaluate a child's emotions or mood on the child's normal behaviour. Thus, they are able to make an assessment if this is the child's normal emotionally state or if it has changed (Chapter 4). This would be more difficult to assess in a very young infant when the caregiver has not yet established the child's normal. Comments from the experts revealed an assessment of mood to be based on 'alertness' and 'interaction with caregiver and environment' but 'may be irritable when tired or hungry' (Table 10-42). Examples of emotions are given by the experts as happiness or unhappiness, sadness and crying (Table 10-42). The ICF-CY classifies emotion as a body function as it is thought to relate to mental functioning which brings about a person's disposition as well as the processing of events [105].

A dimension of emotion was included in nine of the fifteen generic HRQoL measures reviewed (Chapter 3). This may be due to the fact that the development of emotional regulation in infancy and early childhood reflects the strategies used into adulthood [107], [109], [194], [268]. Genetic, environmental and experience factors all contribute toward brain development which in turn shapes social emotional development [194]. Early experiences including the interaction between caregiver and child play an

imperative role in the development of infant mental health and emotional competencies [194], [268]. There is a wealth of evidence to suggest that both acute and chronic experiences of negative emotions have instant and prolonged detrimental effects on many of the body's systems including: neuroendocrine, autonomic and the immune system [107].

The infant is able to identify emotion from birth by selecting important information displayed on human faces and through their voices. Infants prefer to look at faces and thereby engage with caregivers with eye gaze. Infant are able to distinguish, differentiate and imitate facial expressions displayed by their caregivers. Infants are able to interact through auditory expression as well but this is usually coupled with facial expression [194]. Regulation of emotions is shaped in the infant through the caregivers caring verbal and facial response to changes in the child. The caregiver's voice is essential not only to the infant's ability to regulate but also to their level of attention and state of arousal [194]. Infants are able to discriminate happy expressions from other emotions and from the age of 7 months they begin to change their attention from happy faces to faces which express fear. By 10 months of age infants are able to distinguish between a range of positive and negative facial expressions. Toddlers between 18 and 21 months start to develop awareness of their own emotional state and are able to express emotions such as shame, guilt and pride [194]. The maturation of emotional regulation is closely linked to the development of cognitive skills, language and motor control allowing for greater interaction with the environment [194].

Emotion and communication are both dependent on the interaction between the carer and the child. Emotion is further dependent on communication as it makes use of both verbal and non-verbal signs. Communication may be arguably used as a proxy for emotional development, especially in the very young child. The expression and thus interpretation of emotions in very young children is largely unclear and children only start to develop an awareness of their own emotions later in life. Experts in the field have further alluded to the fact that expression of unhappiness such as crying may be due to hunger, fatigue or discomfort and not from emotional distress. Thus the regulation of emotions is possibly more important across the age group of 0-36 months and would be influenced by both the child's emotional control as well as the input given from the caregiver. This is further affirmed by the ICF-CY definition of emotion which includes the processing of events which would, in older children, culminate in an expression of emotion. The term 'regulation' was thought difficult for caregivers of differing educational levels to understand and the synonym of 'control' was sought. The emotional control or regulation seems to be dependent in this age on the verbal and non-verbal cues from the caregiver or familiar people as well as familiar aspects of the known environment. After much debate the descriptor for emotions was based on the regulation of emotions rather than the expression of emotions and was described as: 'settles easily with familiar people, touch or sound'.

5.5.3.6 Movement

Movement or physical functioning was included in all 15 generic HRQoL measures reviewed (Chapter 3). Similarly, movement was ranked as important for all age groups by experts in the field. The reasoning behind the importance of movement includes giving an indication into the child's overall health condition as well as presence of disability or pain (Table 10-43). The ICF-CY has an entire chapter dedicated to movement and includes functions of joints, bones, reflexes and muscles which are necessary to carry out the complex task of movement [105].

Movement is an essential part of a child's emotional and physical development. Children learn about themselves and the world around them through exploring, practicing and mastering physical movements and skills[269]. Through the years many theories of motor development have emerged and it has become evident that genetics and environment both contribute toward gross motor development [110], [111]. Globally there is agreement on the order and timing of motor development. The repertoire of movement from birth to one month is limited and comprises of the ability to grasp, suck and wide range movement of the arms and legs when awake [194], [247]. From 2-5 months control of the neck muscles becomes more evident with the ability to lift the head in prone, visual tracking of objects and the initiation of rolling initiated by the head [194], [247], [270].Between 6-7 months most children develop sufficient trunk control to begin sitting independently and crawling emerges around 9 months [247].From 11 months postural control evolves again with the ability to cruise along furniture [194], [247], [270]. Independent walking typically starts between 12 and 18 months of age [194], [247], [270]. Gross motor skills evolve through practice and different experiences contributing to advancement in motor memory, recognition of actions, control and planning of movement [194]. Walking remains the most effective means of movement between places into adulthood.

Movement can be considered quite similar to communication where there are quite definite age ranges in which it is expected to acquire certain skills and resultant movement patterns. Although this is influenced by the environment and genetic factors there is global agreement on a basic timeline for acquisition of movement. The descriptor for the dimension of movement is thus suggested as: '(0-1 months" grasping, sucking) (2-5 months: plays while on tummy) (6-7 months: sitting) (9-11 months: crawling and standing) (12-36 months: walking)'. All of the movements described are observable.

5.5.3.7 Pain

Pain was a well engaged dimension in both of the cognitive interviews and Delphi study. Caregivers felt that the dimension of pain was essential in all children aged 0-7 years of age. The impact of pain on the general health of the child is clearly demonstrated in regression analysis, even in children under three years of age (Table 4-14, Chapter 4). The importance of pain as a determinant of HRQoL was echoed by the experts. Pain is defined as a sensory and emotional occurrence which occurs due to potential or actual damage to a structure of the body [105], [271]. Pain behaviour was judged by caregivers on behaviours such as grimacing, inconsolable crying, inability to play and/or sleep and poor emotional regulation. This was similarly described as experts as the persistence of the child's crying, their interaction with the environment, facial grimacing or general discomfort. This is similar to infant pain behaviours of facial expression, body movements and crying, discussed in literature [232], [271]. Experts do however; further remark that pain is non-specific in younger children and one relies on the caregiver to determine whether the child is expressing distress due to pain or other issues such as hunger or tiredness.

Pain is a subjective experience and is determined by an individual's physiology, experiences and social and cultural environment. A child under the age of three has not yet developed the cognitive and language skills to assess and express the nature and intensity of pain for evaluation [34], [35]. Thus, we rely on the caregiver's report of the child's pain. Caregivers have the greatest exposure and insight into a child's behaviour and will also determine health-seeking behaviour [232], [271], [272]. It is however, difficult to ascertain whether the behaviours described by caregivers can be attributed to pain or other features of physiological or emotional distress [232], [273]It is thus suggested that one also measures whether the infant's crying is directed toward a nearby person and the ease with which the child calms with comfort measures (pacifier, rocking, touch, verbal reassurance or offer of food) [232], [273]

Many pain assessment scales have been developed for use with preverbal children as these children are at high risk of having unidentified or inconsistent assessment of pain and subsequent inadequate pain management[233]. The Faces, Legs, Activity, Cry, Consolability (FLACC) Observational pain scale is a valid and reliable measure of pain for children with all disease types as well as children with special needs up to the age of 7 years [233]. The FLACC scale is measured on a scale according to the presence of behaviour of the Face, Legs, Activity, Crying and Consolability.

There is a wealth of research available on the observable behaviours associated with pain. These behaviours have been considered and have tried to be presented to the caregiver in the most concise and

comprehensive manner. The suggested descriptor is: 'painful behaviour includes: grimace, restless movement, inconsolable cry.'

5.5.3.8 Play

Play can be categorized as the occupation of a child, with play being the preferred way of engaging with the world [236]. This was identified by both the caregiver's and the panel of experts in the. Experts further suggested that play is the means through which children learn, explore and interact thus, enhancing sensory, cognitive, social and motor development. The experts further explained that the repertoire of play was dependent on the age and acquisition of gross and fine motor skills. Play is initially initiated and dependent on the caregiver or objects placed strategically in their environment, as children advance with age and skills children master playing independently and then alongside children and then together with other children.

This is strengthened by the literature which explains that play in early childhood is associated with cognitive, linguistic, socio-emotional, problem-solving and identity development [236], [274]. Play is considered a major life area of activity and participation of the ICF-CY [105]. Play is thought to assist in acquisition of skill, the development of social relationships as well as a form of recreation [105].

Children participate in a wide variety of play across the lifespan which all create different learning opportunities for the child, these include: exploration through play, expanding the capabilities of current skills and abilities when immersed in play, development of social connections as well as development of emotional regulation through role-play with play partners or bystanders [274]. Child play follows a progressive developmental trajectory. A child enters the sensorimotor or non-symbolic phase of play during the first year of life, this is characterized by exploration of objects which leads to an understanding of the physical qualities the object possessed, the function of the object and the effects which they can produce [275]. At 12 months children then move into the phase of symbolic or pretend play which is thought to have a key role in cognitive and language development. In the first stage of symbolic or pretend play the child is able to use a toy object in the way that the real object would normally be used, for example pretending to speak on a toy cell phone. Later in this stage they are able to use a non-related item to represent another item e.g. Pushing a box as though it were a car [275].

There are six different stages of play throughout childhood [276]. Unoccupied play typically occurs in the first year of life when the child observes people, play and objects more than he/she plays. Around 12 months of age the child normally develops solitary/independent play and the child will play on his/her own

and focus on the activity. At two years of age children begin engage in parallel play, where they play independently but within a social group. They often observe what the people around them are doing and mimic their actions. Associative play emerges around three years of age and children are more interested in the people playing. They may play with the same toys and discuss what they are doing but they don't work together at the same game. Playing together in an organized activity or game is known as cooperative play. This typically emerges from about five years of age. Participants in the game will have an assigned role and rules are made for the game or activity [276].

It is evident that play in childhood, as with other higher functions, develops along a trajectory with increasing complexity as the child develops. From the literature it is clear that children only start to engage in play behaviour with other children after the age of three. Although they would happily play alongside peers and mimic their actions before then. Thus, play for children under three years of age should focus on their playful interaction with toys or objects rather than people. The play behaviour displayed toward toys or objects varies immensely with age and exposure. Play is seen as the occupation or ADL of a child and one which they get pleasure from. The descriptor for play was suggested as 'enjoys playing with objects or toys'.

5.5.3.9 Relationships

A dimension described by social interaction or relationships was included in 11 of the 15 generic HRQoL measures for children under the age of seven years (Chapter 4). Furthermore, relationships and social interaction was found to be important from the cognitive interviews, meeting with a panel of experts and the Delphi study [86]. Experts, from the Delphi study, describe relationships as the bond between mother and/or family and the child. Relationships were also seen as an indicator of emotional wellbeing, cognition and communication. Relationships are coded in the ICF-CY as an activity and participation as it is deemed an interaction with other people in a socially and culturally appropriate manner. These relationships can be between familiar or unfamiliar people, between family members and between caregiver and child [105]. According to the psychological attachment theory the relationships which are formed in infancy effect relationships across the lifespan [114], [258], [277]. Early caregiver-child attachment also forms the basis for motor, cognitive and emotional development [107], [258], [277].

Gaze is the most important approach of interpersonal exchange throughout the lifespan. Shared gaze is an indication that there is a willingness to interact whilst a break in gaze signals the end of the interaction [278], [279]. The rapid development of visual attention in the first 3 months of life allows for caregiver-infant interaction and attachment which shapes the child's ability to infer the caregivers thoughts and

feelings [279]. This is thought to be determined by genetic factors in which the child's behaviour influences the caregivers response as well as the fact that environmental factors of people's interaction with the child determines the child's social development[279]. Identification of another person's thoughts and feelings is necessary for social interaction[279]. Development of communication with reciprocal auditory interaction lays the foundation for future social communication through language [115], [194].

Children under three years of age participate in parallel play where they play next to a peer and will often mirror what the peer is doing but not engage in interactive play [276]. Relationships develop with those in a caregiving role or with family members who are in close regular contact with the child. This relationship develops with the child's interdependence on the family for activities of daily living and need to indicate when assistance is required through verbal or non-verbal communication. Due to the close relationship between the child and family members this is often carried out seamlessly[119], [235]. Health infants and toddlers can spend up to 11 ½ hours eating per week. This is an opportunity for socialisation and development of relationships not only between the infant or child and the caregiver but also with the family[263].

Psychological development is intertwined with the development of communication, behaviour and relationships. In the infant and with some toddlers these dimensions could act as proxy for each other. Due to the fact that relationships develop with close caregivers or family members this should be the essence of the dimension. In both play and psychology research the importance of engaging with peers or other children appears mostly after the age of three years. The dimension descriptor is thus suggested as: 'interacts with family members in an age-appropriate manner).

5.5.3.10 Sickness

Sickness was considered, by the experts, to be any form of illness or other contributing factor leading to poor health that would negatively impact on the HRQoL of the child. This was similarly, the reasoning behind the scoring of the EQ-5D-VAS by caregivers during the cognitive interviews. Thus, sickness would be better described by "General Health" which would also correlate to the dimension of general health which was included in 4 of the 15 HRQoL measures reviewed. This would correspond with the ICF-CY component of activity or participation in maintaining health. This would include the awareness of maintaining health as well as responding appropriately to poor health by seeking professional assistance [105].

The recommendation would thus be to not incorporate it into a dimension of the HRQoL measure to be answered with a Likert-type scale as this would give a very narrow focus of general health. This dimension

is more accurately measured by the EQ-5D-VAS on a rating scale of 0-100 which will thus be incorporated into the new measure.

5.5.3.11 Sleeping

Sleep was described by the experts as essential for growth and development of the child. Furthermore, poor sleeping patterns in a child leads is thought to reduced sleep in the caregiver which could result in the quality of the caregiver-child attachment (Table 10-48). Sleep was an important determinant for caregivers in rating their child's pain, emotional status and their ability to play or partake in usual activities during the cognitive interviews (Chapter 4).

Poor sleeping is said to be one of the foremost concerns for parents [256]. Sleeping is assessed by caregivers on the ability to fall asleep, uninterrupted sleep and the duration of sleep over a 24 hour period. There is a wealth of research in agreement with the experts, from the Delphi study, in highlighting the importance of sleep for child development. Poor sleep in childhood has been linked with anxiety, behavioural problems, impaired cognitive development, obesity and language delay [280], [281]. Initially infants spent 16- 20 hours sleeping over a 24 hour day, 15-16 hours of sleep for a 3-6 month old, 11-14 hours between 6 -12 months old and, 10-13 hours for a toddler between 1 and 3 years and 7 hours in a 24 hour day by adulthood [281]. In childhood napping during the day has shown to improve learning with a consolidation of learning before the nap. Similarly a good night's sleep has shown to consolidate everything that the toddler had learnt during the previous day[281].

The ability to sleep without disruption is influenced by: the child's temperament and health; their physiological make-up; the family practice and routine; the sleep environment; and the sleep schedule [282].

Sleep is very important for both the caregiver and the child. A long term reduction in sleep or poor sleeping pattern has negative effects of both the child and the caregiver. In terms of measuring HRQoL for the period of 'today' it can be argued that one night of poor sleep may or may not have a sizeable effect on HRQoL. Sleep in young children is more often than not unpredictable and may be of more concern to the caregivers than the child. Although sleep may be greatly affected by the health of the child this may not always be the case. The dimension of sleep will need further testing in the new measure to ascertain the value of its contribution toward the measurement of HRQoL. The descriptors of sleep are based upon the suggestion by both the literature and experts in the field: 'falls asleep easily, has restful uninterrupted sleep and enough sleep. (0-3 months: 16-20 hours a day) (3-6 months 15-16 hours a day) (6-12 months: 11-14 hours a day) (12-36 months: 10-13 hours a day).

5.6 Discussion and Conclusions

The two rounds of the Delphi study culminated in significant pruning of the item bank. The suggested age range for inclusion was however not well established through the first round of the study. As seen in Figure 5-1, age groups of 0-3 years and 1-3 years were selected equally. Due to the fact that the top ten items were equivalent for CVI and weighted totals across the three age groups, the decision was made to develop a measure for children aged 0-3 years. The additional three items of behaviour, communication and independence were rated as important for the older children in the age group by experts in the field. The decision was made to include these three items and word them with age-appropriate descriptors as caregivers did recognise the importance of these items in the cognitive interviews. These items would be tested on the Alpha Draft and if the results showed that they did not perform well across the age groups they would be excluded. Alternatively it may be found that different versions may need to be developed for different age groups of children between the ages of 0-3 years. As a number of the items were selected as important across age groups it may be possible to develop one instrument which would perform well across the age groups.

The participation in the second round of the Delphi study was poor. This could have been due to the relatively long length of the survey and the associated cognitive burden. Many of the items were duplicated across age group would culminated in the expert repeating a lot of their thoughts. Although this is one of the limitations of the results it was important to establish: 1) whether items were in fact ranked similarly across age groups, 2) whether the reason behind the selection of each item was equivalent across age groups and 3) how the descriptors differed across age groups. These answers have assisted with the selection of items, subsequent dimensions and the formulation of the dimension descriptors. It has given further insight into how we expect the first draft of the new measure to perform.

It was suggested that independence in young children is manifested in their ability to assist with activities of daily living such as washing, dressing and toileting. Thus the decision was made to reword the item of independence in the new measure to “assisting with daily activities.” In keeping with the wording of the EQ-5D-Y Proxy the item of play was renamed to playing. The item of emotions or mood was found to centre on the child’s ability to regulate their emotions either internally or externally thus; the item was renamed to emotional regulation. The word regulation was considered to be difficult to understand and thus controlling emotions was used instead. The item of sickness related to the general health and well-being of children and is thus captured on the EQ-5D-Y VAS.

The ten dimensions of behaviour, communication, eating, independence (self-care), emotions, movement, pain, play, relationships and sleeping will be included in the Alpha Draft of the measure for further testing. The dimension of sickness will be measured by the VAS in the question regarding the child's health today. The ten dimensions and their descriptors were validated against the literature. The items of behaviour, emotion and relationships are interlinked and evolve from the same psychological phenomenon of attachment and reciprocal interaction. One of the considerations for all of these dimensions is the importance of the dimension to the HRQoL of the caregiver as opposed to the HRQoL of the child. This would need to be further investigated by determining the interaction of the HRQoL of the caregiver when the instrument is tested.

The item selection was considered within the conceptual framework of the modified ICF. The items should reflect all categories within the ICF (with the possible exception of environmental factors) in order to assess HRQoL holistically. It is evident that the items could represent a number of ICF-CY descriptors depending on the description of the item in the measure. As the instrument aims to be a HRQoL rather than a general QoL instrument, it is may not be surprising that environmental factors are the least represented. The inclusion of external factors, such as building accessibility and policy regarding health and wellness related issues may very likely influence HRQoL, much as the health condition might. However it is rather the perceived impact of these components of the ICF on the HRQoL of the respondents, rather than the factors themselves that needs to be included. As personal factors are not codified in the ICF and generally include demographic details such as age and gender, these are also not represented here.

The limitations of this study include the small number of respondents who completed the first and subsequent round of the Delphi Study. This further limited the statistical analysis and conclusions which could be drawn. The selection of participants was limited to experts who were known to the research group which introduced a selection bias and further limited the results as experts from sectors such as social work and education were not invited to participate. This limitation was diminished by the fact that all of the experts who participated work within a multidisciplinary team. Of note the developmental paediatrician works together with the education department in determining school readiness and placement of children.

In conclusion, a bank of items was selected based on the findings from the literature reviews, cognitive interviews, Delphi study and workshop with experts in the field. This process ensured that the items and subsequent dimensions for inclusion were developmentally appropriate for the age range of inclusion. The final dimensions included: behaviour, communication, eating, independence, play, emotions, movement, pain, relationships, sickness and sleep. These dimensions were representative of the definition of HRQoL and encompassed broader dimensions of physical (eating, play, movement, pain, sickness and sleep),

emotional (behaviour, communication, emotions) and social (behaviour, communication, independence, relationships). These items are also representative of the dimensions of the ICF: body structure and function, activities and participation.

6 Chapter 6: Finalisation and Testing of the Alpha and Beta Drafts

The rigorous process of candidate item identification and pruning resulted in ten dimensions and a general rating of health on the VAS. These items now had to be operationalised, utilising the descriptions provided by the panel, and the questionnaire had to be drawn up and formatted before pilot testing could be done. Careful consideration needed to be given to the descriptors of the item as the intention is that one questionnaire would be valid for the entire age spectrum between 0-36 months. Thus, we are hoping to develop a 'one-size-fits-all' instrument.

6.1 Alpha Draft Design

The Alpha Draft HRQoL-6D- IT is presented in Appendix 13.

6.1.1 Content

Dimensions were operationalized with a description of the observable behaviour which was drawn from suggestions from the Delphi study and the literature. The descriptors of the dimensions have a maximum Flesch-Kincaid readability level of seven to ensure comprehensibility [283] . Careful consideration was given to whether the dimensions should be criterion or norm referenced. The results from the cognitive interviews (Chapter 4) indicated that caregivers referenced dimensions of Mob (48%), UA (41%) and SC (39%) to other children and their child's own behaviour quite similarly. Criterion reference increased slightly when one only considered children under 36 months of age: Mob (53%), UA (41%) and SC (50%). Results from the mapping review (Chapter 3) indicated that inclusion of criterion referencing could be one way of increasing the observability of the dimension. Another method of increasing observability would be to compare the child's behaviour to the accepted developmental milestones for their age. The inclusion of age appropriate descriptors across the age band was postulated to increase the applicability of the dimensions across the different ages thus ensuring a 'one-size-fits-all' instrument and was thus implemented in the Alpha Draft.

6.1.2 Layout

Questions regarding the layout of the EQ-5D-Y Proxy were included in the cognitive interviews with caregivers. The layout was thought to be clear, logical and easy to read. Thus, the layout of the EQ-5D-Y

Proxy was retained for the Alpha Draft, with the permission of the EuroQoL Foundation. In keeping with the EQ-5D-Y the dimensions were re-arranged as follows: movement; assisting with daily activities, playing, pain, controlling emotions, relationships, behaviour, communication, eating, sleeping and the VAS. This further allows for minimisation of bias with emotional questions not being presented first [134]. The instructions for proxy completion were provided on the front page with a clear explanation that the dimensions should be completed from the viewpoint of the proxy not the child, in keeping with the conceptual framework (Chapter 2). The font of Comic Sans size 12, used on the EQ-5D-Y Proxy, was well received during the cognitive interview with caregivers. There were no suggestions to change the font. Thus, the font was retained for the Alpha Draft. There was only one dimension on the EQ-5D-Y Proxy 'usual activities' which included additional information in parenthesis. This information was displayed in Comic Sans Italics size 12. Due to the additional qualifiers needed for all of the dimensions of the Alpha Draft this information was displayed in parenthesis in Comic Sans Italics size nine. The VAS was retained with the wording, layout and font from the EQ-5D-Y Proxy.

6.1.3 Length and Time Frame

The results from the literature reviews, cognitive interviews, Delphi study and workshop with experts in the field all concluded that a short concise measure was favourable, particularly if preference weights were to be developed in the future. The EQ-5D-Y Proxy format with five dimensions was commended for its ease of administration and high clinical utility. The Alpha Draft included ten dimensions (+ the VAS) which were to be reduced after testing. Ideally the measure would have five to seven final dimensions.

The EQ-5D-Y Proxy is the only HRQoL measure which uses a time frame of 'today'. This reduces the effect of recall bias and makes valuation exercises easier [86]. There were suggestions from the workshop with experts in the field that the recall period should be changed to yesterday as that would be a full account of a day [86]. 'Today' was criticized as the period of assessment would be dependent on the time of the day that the measure was administered [86]. Giving consideration to the variability in infant's behaviour it was further suggested that the time period of a week was given [86]. However, during the cognitive interviews the time frame of 'today' was accepted and not criticized by those answering the EQ-5D-Y Proxy. If the new measure has the future possibility of valuation for preference weighting to allow comparison with the other EQ-5D versions, utilising the same time frame of 'today' would be advantageous. Thus the time frame of 'today' has been retained from the EQ-5D-Y.

6.1.4 Response Options

The EQ-5D-Y Proxy version has three levels of report [36]. The EQ-5D, (adult version for self-completion) has two versions available: one with three levels of report and one with five levels of report [267]. The three level version was expanded to five levels in an attempt to improve the responsiveness of the questionnaire.–Inclusion of five levels of report decreased the ceiling effect and thus increased the responsiveness of the instrument [267] .However the improved responsiveness of the instrument with five levels of report is reported by at least one author to have compromised the reliability of the instrument [268]. Caregivers who participated in the cognitive interviews (Chapter 4) reported that the Likert response options in the EQ-5D-Y Proxy were easy to understand and rank. Thus response options from the EQ-5D-Y Proxy were implemented in the Alpha Draft and describe: no problem, some problems, or a lot of problems.

6.2 Testing of the Alpha Draft

6.2.1 Aim and Objectives

The primary aim of this study was to reduce the number of dimensions for inclusion on the Beta Draft.

The specific objectives were to determine:

- The applicability of the dimensions as determined by the caregiver's responses.
- The responsiveness of the dimensions by evaluating the response patterns for floor and ceiling effects.
- The reliability of the scale and individual dimensions using the Cronbach's Alpha.
- The known group or divergent validity between the AI and TD children using the Fisher Exact test for the frequencies of responses to each level.
- Dimension equivalence across the age groups through examining the proportion (plus 95% confidence intervals (CIs)) of problems which were reported.
- The structure of the questionnaire which was examined using exploratory factor analysis.
- The structure of the questionnaire in terms of severity, dimension monoticity, the usefulness of the information and the order of the thresholds using IRT.
- Known group validity with the VAS scores of the new measure.
- Which dimensions influenced the VAS scores through regression analysis.
- Whether the VAS scores were correlated to age by testing for heteroscedasticity.

6.2.2 Methodology

A correlation descriptive design was used. This section of the research explored the dimensions included in the Alpha Draft. The proposed research settings included a tertiary paediatric hospital and a day-care centre at the hospital which accepts children of the employees of the hospital.

6.2.2.1 Participants

The participants included caregivers of children aged from birth to three years. Caregivers of children under three years who attended a day-care centre (TD children) or who accessed acute health care services (AI children), 24 hours or later post admission were included in the study. A caregiver of the child was defined as any person over the age of 18, who lived with the child and was wholly or partly responsible for the care of the child's physical and emotional needs e.g. mother, father, aunt, uncle, grandparent, brother or sister.

Caregivers who were unable to speak or understand English were excluded as the study was developing an English proto-type instrument before translation into other languages. Caregivers of children who were medically unstable, terminally ill or who were born prematurely and had not yet reached their corrected age of birth were excluded from the study. An unstable child was classified as any child who was less than 24 hours post admission to ICU, less than 24 hours post-surgery or any child who had any acute changes in their medical condition.

Caregivers of unstable, terminally ill or recently admitted children (less than 24 hours post admission) were excluded to limit the emotional stress that these participants would be subjected to. Children who had not yet reached the corrected age of birth were excluded due to the time period needed for them to catch up to age appropriate developmental milestones.

6.2.2.2 Sample Size Determination

The sample size determination proved to be challenging as it was not known how the caregivers would respond to the dimensions. If one considered the reliability of the scale, and the resultant effect on the overall reliability of the scale if a dimension was removed, it was decided to consider the sample size based on Cronbach's Alpha which was found to be high (0.83) on other EQ-5D instruments [284]. It has been shown that the coefficient alpha is not only dependent on the sample size but also on the largest eigenvalue of the sample data set. According to Yurdugül (2008), if one sets the first eigenvalue between 3.00 and 6.00 the minimum sample size of n=100 is sufficient for an unbiased estimator of coefficient

alpha [285]. Furthermore, when analysing factor analysis based on the correlation matrix of the variables one usually needs a large sample size. It is suggested as a rule of thumb, that at minimum ten observations is needed per variable [286]. Due to the fact the Alpha Draft had ten dimensions a sample size of 100 would be needed. It was thus decided that the maximum sample size needed was 100. This was divided between AI and TD children with a minimum of 50 participants in each group.

6.2.2.3 Instrumentation

The Alpha Draft was administered to participants and consisted of ten dimensions namely: movement (mvt), helping with daily activities (daily activities), play, pain, controlling emotions (emo), relationships (rel), behaviour (beh), communication (comm), eating and sleeping. The Alpha Draft was given the name of the HRQoL-10D-IT (Infant and Toddler), as it is a HRQoL measure with ten dimensions available for Infant and Toddlers (Appendix 13). The HRQoL-10D-IT will be referred to as the Alpha Draft.

6.2.2.4 Procedure

Ethical approval was obtained from the UCT HREC (HREC/REF: 336/2014) (Appendix 2) and the children's hospital (Appendix 14). Permission was gained from the EuroQoL Foundation to use the layout and wording of the EQ-5D-Y and an intellectual property agreement was signed.

The caregivers of AI children in the general medical ward of the children's hospital were invited to participate in the study. Participants were first recruited in the B1 and then B2 medical ward from the first cubicle to the last cubicle in numerical order in each of the wards. The details of the study were provided to participants in writing and explained by the researcher (Appendix 15). Informed consent (Appendix 15) was taken, from willing participants who met the inclusion and exclusion criteria, 24 hours or later, post their child's admission to the acute hospital. With the assistance of the researcher caregivers were asked to complete Alpha Draft (Appendix 13). This was done in a private counselling room or at their child's bedside if the caregivers preferred. The interviewer noted any concerns regarding comprehensibility of the dimensions and comments on the general layout of the measure. Completion of the measure did not take longer than ten minutes. No additional information was recorded as the aim was to assess the performance of the Alpha Draft dimensions only.

Caregivers of TD children from the day-care centre were identified from a list supplied by the day-care centre which detailed the children's names, date of birth, responsible caregiver and the department in which they worked. On the recruitment days the caregivers who were on duty at work were approached

given the details of the study and invited to participate in the study (Appendix 15). Informed consent (Appendix 15) was taken and caregivers were asked to complete the Alpha Draft (Appendix 13) with the assistance of the researcher, at a time and place convenient to them. The researcher was present during the completion of the Alpha Draft to assist if necessary. The interviewer noted any concerns regarding comprehensibility of the dimensions and comments on the general layout of the measure. No additional information was recorded as the aim was to assess the performance of the Alpha Draft dimensions only.

6.2.2.5 Data Management

The answers given on the Alpha Draft was entered into an Excel spreadsheet for statistical analysis. The consent forms and completed copies of the Alpha Draft were stored in a locked office. No identifying information was recorded on the Excel spreadsheet or for any other analysis.

Age range of the children for inclusion was between 0 – 36 months. To ensure that the instrument was applicable to children across this age band, three age groups were assessed during data analysis. The age groups were divided as follows: birth <1year (0-12 months); 1<2years and 2<3 years (24-36 months).

Descriptive analysis to determine frequency of problems, acceptability, and responsiveness was done on SPSS version 23. Reliability and Factor Analysis was performed in Statistica version 13. Vassarstats (http://vassarstats.net/) was used to calculate Fisher Exact scores, probability scores and 95% confidence intervals. Small Stata version 14 was used for IRT analysis.

6.2.2.6 Statistical Methods

Frequency (ordinal data), median (ordinal and categorical data), range and mode (categorical data), were used to describe the data. The Shapiro-Wilk Test (numerical data from the VAS) and the Kolmogorov-Smirnov test (ordinal data) tested the normality of the data. Non-parametric tests (median and Spearman's rank correlation) were utilised for ordinal and non-normally distributed data. Parametric tests (mean, standard deviation and Pearson's correlation co-efficient) were utilised for normally distributed numerical data. The Fisher exact scores were calculated to determine significant independence between dimension scores of AI and TD children and across age groups. The distribution of frequency of dimension scores across condition groups was used to determine the responsiveness of the dimensions in terms of ceiling and floor effects. Reliability of the questionnaire and dimensions was established through Cronbach's Alpha. The dimensions were assessed for their equivalence across the age groups through the proportion of no problems which were reported and the 95% confidence intervals. Kappa was used to determine if there

was any correlation between dimension scores. Varimax Rotated Factor Analysis was used to examine the structure of the questionnaire and determine the variance each of the factors contributed to the scale. The structure of the questionnaire was further examined using IRT to determine: individual dimension severity, dimension monotonicity, the usefulness of the information and the order of the thresholds. To distinguish if there was any difference between VAS scores between AI and TD children analysis of variance (ANOVA) was used. Post Hoc Analysis was used to identify VAS means for AI and TD children, who were different from each other. Regression Analysis of the VAS scores was used to determine the effect that the dimension scores had on the VAS. The level of statistical significance was set at $p \leq 0.05$.

6.2.2.7 Ethical Consideration

Ethical principles of autonomy, confidentiality, beneficence/non-maleficence and justice applied in the testing of the Alpha Draft are detailed below and were based on the Helsinki Declaration [243].

Autonomy

Prior to commencement of the study, consent was obtained from the children's hospital where the study was to take place (Appendix 14). All participants who met the inclusion and exclusion criteria were given an information pack which detailed the purpose of the study, their role in the study, the risks and benefits, the confidentiality of their information and their right to refuse to partake in the study or withdraw at any point. This information was further explained by the researcher, if any clarification was needed. Thereafter informed consent (Appendix 15) was obtained from each of the participants who had given consent of their own free will.

Confidentiality

None of the children's or caregivers names were recorded during the study. The only identifiable information was the signature of the caregiver used during consent. The confidentiality of each participant was maintained by keeping the information in a secure locked cupboard. The electronic files were password protected on a secure computer.

Beneficence and non-maleficence

The data collection did not affect the medical treatment which the child received or the way in which the caregivers were perceived at the health institution. The participants did not incur any costs for their involvement in the study and thus no monetary re-imbursement was given.

The research had a potential to develop a new HRQoL measure, for very young children, which would be valid and reliable for use in children in South Africa. This would be beneficial in measuring HRQoL of very

young children in the future. This could have assisted in improved understanding of the child's health condition and could improve management thereof.

If any developmental or maladaptive behaviour concern was noted the caregiver of that child would have been consulted and with their consent referral to the relevant practitioner would have been made. No children were identified as having concerns that were not already managed by the relevant health care professional. If any signs of neglect or abuse were noted referral to the necessary authority would have been made, in line with legal requirements. This scenario did not arise. There were no known risks to the participants and therefore no insurance was required for research-related injuries.

Justice

Every caregiver who was eligible to participate in the study was recruited. Caregivers across a range of socio-economic backgrounds were recruited and no-one who met the entrance criteria was excluded on the grounds of ethnic group, gender preference, religion or any other reason.

Due to the fact that a proto-type English version of the measure was being developed only English speaking caregivers were recruited. This limited the eligibility of a great number of the caregivers AI and CI children as the majority of caregivers utilising the hospital's service were Afrikaans or Xhosa speaking.

6.2.3 Results

6.2.3.1 Descriptive Statistics

The participants included 50 caregivers of AI children and 51 caregivers of TD children. Groups of TD and AI were well matched across the age groups in terms of number of participants in each group.

Table 6-1 Age Group of Children According to Condition Groups for Alpha Draft Testing

Age	TD (n=50)	AI (n=51)	Total (n=101)
0-12	14	20	34
12-24	17	16	32
24-36	20	14	34
Total	51	50	101

There were a slightly higher number of children in the AI group in the 0-12 month age group and a corresponding higher number of TD children in the 24-36 month age group (Table 6-1).

6.2.3.2 Acceptability, Layout and Wording of the Alpha Draft

Comments from the interviewer on the acceptability, layout and wording of the Alpha Draft

Most of the caregivers reported that the dimension of helping with daily activities was not applicable due to the age appropriate capabilities of their child. The researcher recorded this in an additional category under helping with daily activities coded as not applicable (N/A) for each caregiver and coded the response as N/A.

Problems with behaviour included that difficulty with behaviour was regarded by the caregivers as an everyday occurrence with children and did not particularly relate to health but unrelated daily struggles. They felt that this was a normal part of childhood and similar behaviour had been noted with their other children or other children who they know. Many of the caregivers noted that when a child throws a temper tantrum it is very difficult for anyone to calm the child and it is best to leave the child to work through it, and not necessarily try to calm them down.

Changing emotional regulation to controlling emotions might have been problematic but this question was understood by all of the caregivers. The tantrums and ‘stubbornness’ of children with tantrums was also considered when answering for emotions. It was felt that there was ‘double counting’ if both problems with behaviour and emotions were included. A relationship with family was a more acceptable question.

Sleeping was a problem which many of the caregivers found amusing and one of the statements recorded was ‘does any child really sleep their required hours of sleep?’ Other comments included that ‘last night was a struggle but the previous night was very good.’

Pain was clearly understood and answered without hesitation for the majority of the caregivers.
Mobility and play were also clear. There was a possible tendency for the caregiver to over report the ability of their child in both of these dimensions based on the discussion that many of them engaged in around each dimension. Communication and eating were generally accepted. A number of caregivers whose children received all nutrition through permanent feeding tubes or gastrostomies were defensive about the question regarding eating. They felt that their child was receiving their nutritional requirements and growing well whether they were receiving it per mouth or feeding tube. Children who were currently nil per month for surgery or investigations were mostly scored appropriately but there was a great emphasis on the fact that the child normally eats well.

6.2.3.3 Frequency of Descriptor Responses and Known Group (Setting) Comparisons - Alpha Draft

As seen in Table 6-2 below the Fisher’s Exact scores indicated that relative proportions of problems are not independent of the presence of acute illness or TD in all dimensions ($p \leq 0.05$) except for behaviour ($p=0.071$). AI children were reported to have more problems than TD children in nine out of ten of the dimensions. A lot of problems were reported in ten instances in TD children, compared to 72 occurrences in AI children. TD and AI children had the same number of children reporting a lot of problems with behaviour.

Table 6-2 Dimension Answers According to Condition Groups on the Alpha Draft

	Typically Developing (n=51)				**Acutely Ill (n=101)**				**Fisher Exact**
	1*	2*	3*	N/A	1*	2*	3*	N/A	
Movement	47	3	0		23	11	16		***<0.001***
	94%	6%	0%		46%	22%	32%		
Daily Activities	25	1	1	24	6	7	4	33	***<0.001***
	49%	2%	2%	47%	12%	14%	8%	66%	
Play	50	0	1		35	9	6		***<0.001***
	98%	0%	2%		70%	18%	12%		
Pain	40	8	3		23	21	6		***0.004***
	78%	16%	6%		46%	42%	12%		
Emotions	39	12	0		31	12	7		***0.015***
	76%	24%	0%		62%	24%	14%		
Relationship	50	1	0		37	10	3		***0.001***
	98%	2%	0%		74%	20%	6%		
Behaviour	36	12	3		25	22	3		0.072
	70%	24%	6%		50%	44%	6%		
Communication	49	2	0		31	12	7		***<0.001***
	96%	4%	0%		62%	24%	14%		
Eating	42	8	1		22	16	12		***<0.001***
	83%	15%	2%		44%	32%	24%		
Sleeping	36	14	1		15	27	8		***<0.001***
	71%	27%	2%		30%	54%	16%		

1: No problem; 2*: Some Problem; 3*: A lot of problems; N/A: not applicable to age of child*

A high percentage of both TD (47%) and AI (66%) caregivers reported the daily activities dimension as not being appropriate to the age of their child. The dimension of daily activity was subsequently not included in any of the statistical tests presented below.

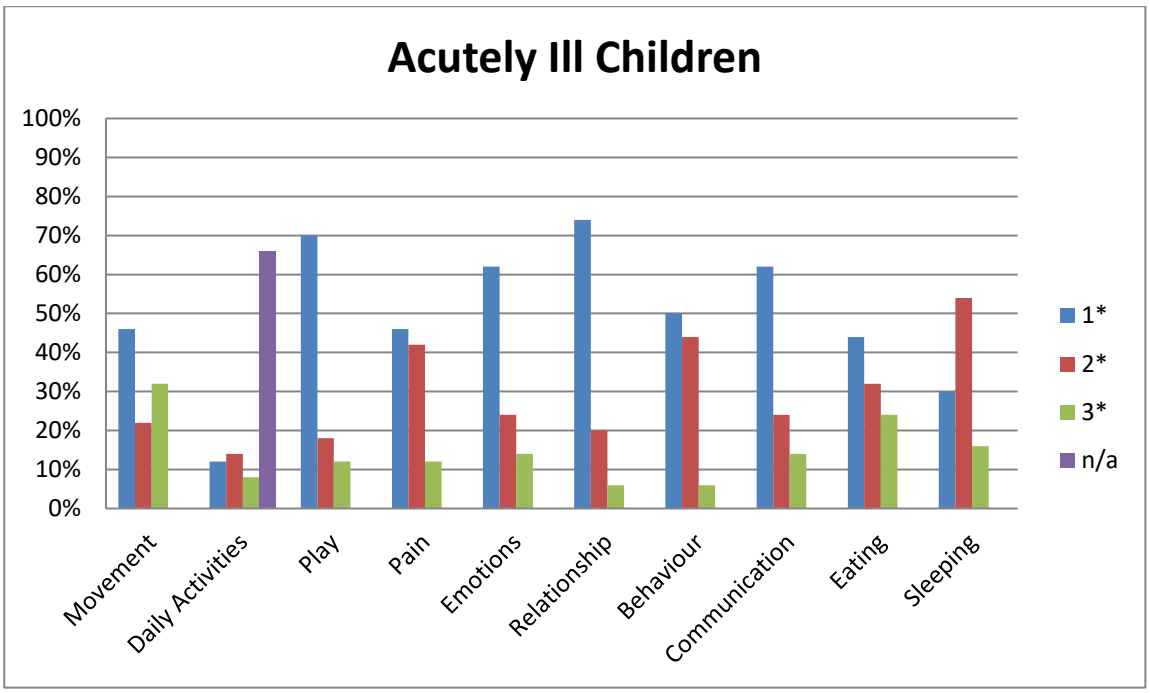


Figure 6-1 Graph Showing the Distribution of Dimension Score Percentages for AI Children on the Alpha Draft

1: No problem; 2*: Some Problem; 3*: A lot of problems; N/A: not applicable to age of child*

As reflected in Figure 6-1 daily activity was a very poorly accepted dimension with many caregivers of TD children (47%) and AI children (66%) deeming the dimension inappropriate. For the group of TD children there was a ceiling effect observed for all dimensions except for daily activities. Ceiling effects were observed in the dimension of relationships (74%), play (70%), emotions (62%) and communication (62%) for AI children. There were no observed floor effects.

6.2.3.4 Performance Across the Age Groups – Alpha Draft

In order to examine the equivalence of the responses to each dimension per age group, the proportion of caregivers reporting some or a lot of problems was calculated (Table 6-3,Figure 6-2). The 95% Confidence Intervals (CIs) of proportions overlap for all dimensions, indicating that the proportion of problems reported in each group is not statistically different but this is likely to be due to the large CIs resulting from the small sample size in each age group. Dimensions of movement, play and sleeping tend to have lower reporting of problem in the older age groups of children. Daily activity, emotion and eating tend to have a lower reporting of problems in younger age groups of children.

Table 6-3 Proportion of Problems Reported on the Alpha Draft for Each Dimension by Age Group

		Mvt	Play	Pain	Emo	Rel	Beh	Comm	Eat	Sleep
0-12m (n=34)	Problems	13	9	11	8	6	12	8	16	19
	No Problems	21	25	23	26	28	22	26	18	15
	Prop with problems	0.38	0.26	0.32	0.24	0.18	0.35	0.24	0.47	0.56
	CI	0.24	0.15	0.19	0.12	0.08	0.22	0.12	0.32	0.39
		0.55	0.43	0.49	0.4	0.34	0.52	0.4	0.63	0.71
12 - 24m (n=33)	Problems	10	3	14	10	3	15	6	10	19
	No Problems	23	30	19	23	30	18	27	23	14
	Prop with problems	0.3	0.09	0.42	0.3	0.09	0.45	0.18	0.3	0.58
	CI	0.17	0.03	0.27	0.17	0.03	0.3	0.09	0.17	0.41
		0.47	0.24	0.59	0.47	0.24	0.62	0.34	0.47	0.73
24-36m (n=34)	Problems	8	4	13	12	5	13	7	11	12
	No Problems	26	30	21	22	29	21	27	23	22
	Prop with problems	0.24	0.12	0.38	0.35	0.15	0.38	0.21	0.32	0.35
	CI	0.12	0.05	0.24	0.22	0.06	0.24	0.1	0.19	0.22
		0.4	0.27	0.55	0.52	0.3	0.55	0.37	0.49	0.52

The older children had a smaller proportion of reported problems across all of the dimensions, whereas the younger age group had a greater proportion of problems reported in all dimensions but pain and behaviour (Figure 6-2). There was a large percentage difference in the proportion of problems reported in movement (25%), play (21%) and eating (28%) between children aged 0-12 months and 24-36 months. Similarly the proportion of problems with sleeping showed a 36% difference between the 24-36 month and 12-24 month age groups.

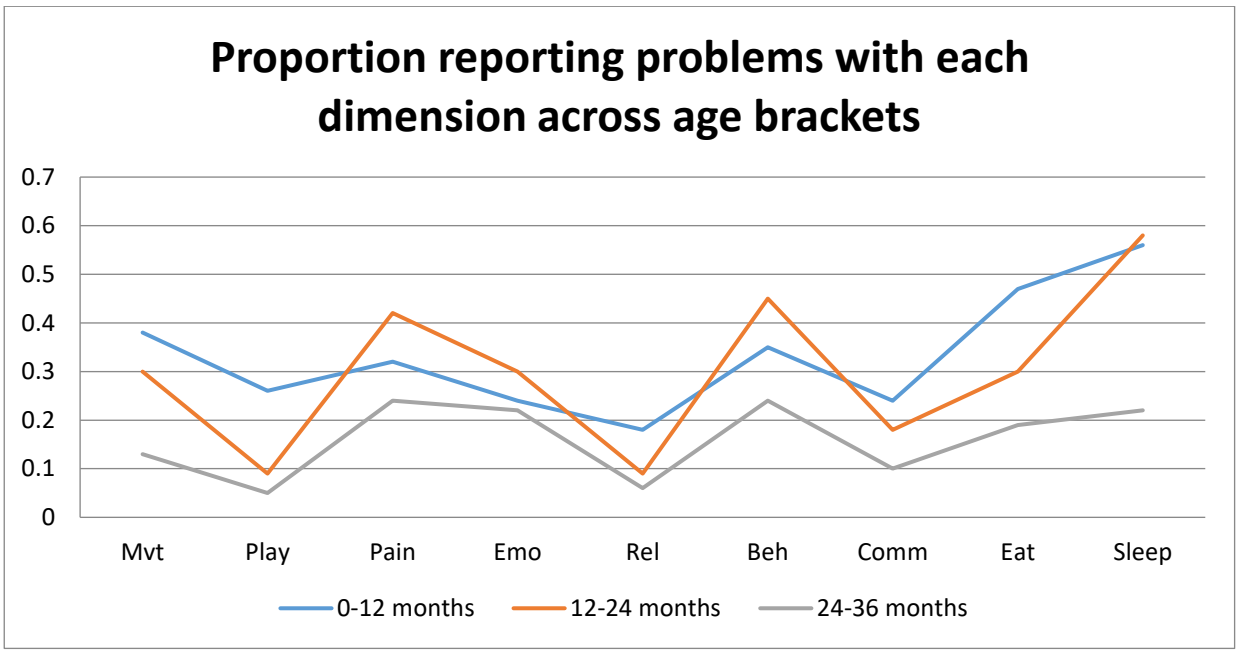


Figure 6-2: Proportion of Children Reported as Experiencing Problems in Each Dimension Across the Age Groups

6.2.3.5 Reliability, Internal Consistency and Factor Structure - Alpha Draft

The reliability of the questionnaire was good α=0.77 [176]. Item-rest correlations show how the dimension is correlated with the scale if calculated from the other eight dimensions. Dimensions which were not well correlated with the scale as a whole include behaviour (0.31) and sleep (0.36) (Table 6-4).

Table 6-4 Internal Consistency and Reliability: Cronbach's Alpha

N=101	**Item-test Correlation**	**Item-rest Correlation**	**Alpha if item is removed**
Movement	0.66	0.53	0.74
Play	0.66	0.54	0.74
Pain	0.57	0.42	0.75
Emotions	0.56	0.41	0.75
Relationships	0.60	0.45	0.75
Behaviour	0.47	*0.31*	0.77
Communication	0.70	0.57	0.73
Eating	0.62	0.47	0.74
Sleep	0.52	*0.36*	0.76
Alpha of the Questionnaire			**0.77**

Daily activities was excluded as it was reported to be not applicable by many respondents

Factor analysis with varimax rotation identified three factors which could be taken to represent: Physical Functioning (activity component of ICF), Social Functioning (participation component of ICF) and Body Functions (Table 6-5).

Table 6-5 Factor Analysis for the Alpha Draft

N=101	**Physical Functioning**	**Social Functioning**	**Body Functions**
Eating	0.84	0.04	0.11
Play	0.75	0.24	0.12
Movement	0.71	0.18	0.22
Pain	0.32	0.05	0.71
Communication	0.31	0.61	0.31
Relationships	0.26	0.73	-0.02
Sleep	0.08	0.09	0.83
Behaviour	0.05	0.73	-0.07
Emotions	0.02	0.60	0.38
Expl.Var	2.03	1.89	1.51
Prp.Total	0.23	0.21	0.17

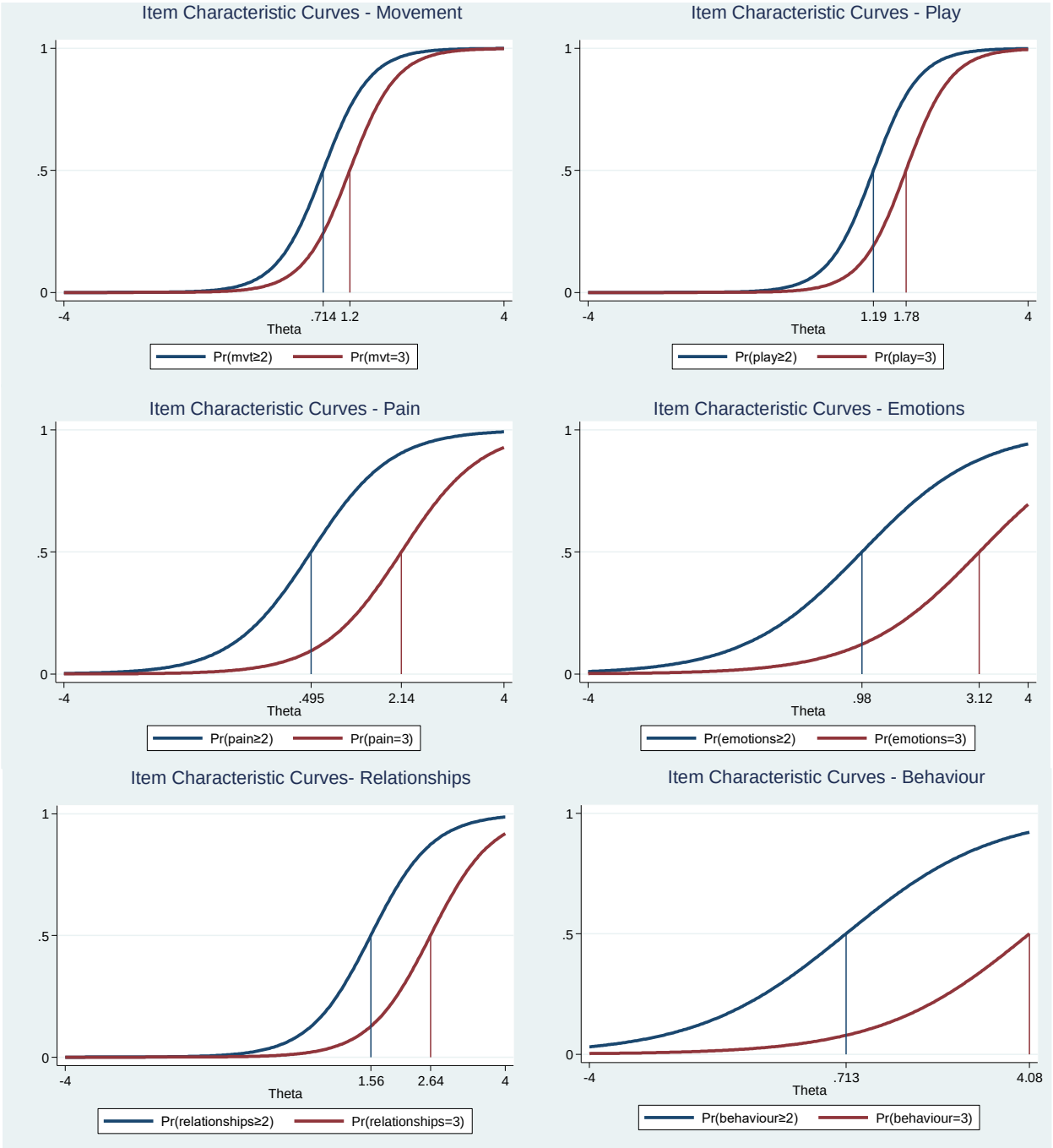
	Eigenvalue	**% Total variance**	**Cumulative Eigenvalue**	**Cumulative% Variance**
Physical Functioning	3.22	35.8	3.22	35.8
Social Functioning	1.21	13.4	4.43	49.2
Body Functions	1	11.1	5.43	60.4

The Physical Functioning accounted for the greatest variance (36%) and included eating, play and movement. Social functioning accounted for 13.4% of the variance and included relationships, behaviour, communication and emotions. Pain and sleep were included in the Body functions factor and accounted for 11.1% of the variance. The three factors combined accounted for 60.4% of the variance of the questionnaire.

6.2.3.6 Item Response Theory (IRT) Analysis – Alpha Draft

IRT analysis was applied to determine how well the different dimensions were able to identify respondents with differing levels of theta, which is the common latent trait, in this case posited to be HRQoL. IRT is dependent on monotonicity, i.e. that there is a common latent trait (HRQoL) measured by the instrument [287]. Although factor analysis did identify different factors, the Cronbach's Alpha was high, thus indicating that the dimensions do measure the same underlying construct, assumed to be HRQoL. In addition, each

dimension showed the characteristic 'S' probability curve [287]. The Item Characteristic curves presented below indicate the point at which there is a 50% probability that the response is likely to move from no problems to some problems and from some problems to a lot of problems related to theta (the underlying characteristic or latent trait). The closer these two points are, the less able the dimension is to discriminate between respondents with similar characteristics. The Item Characteristic curves are presented in Figure 6-3 below.



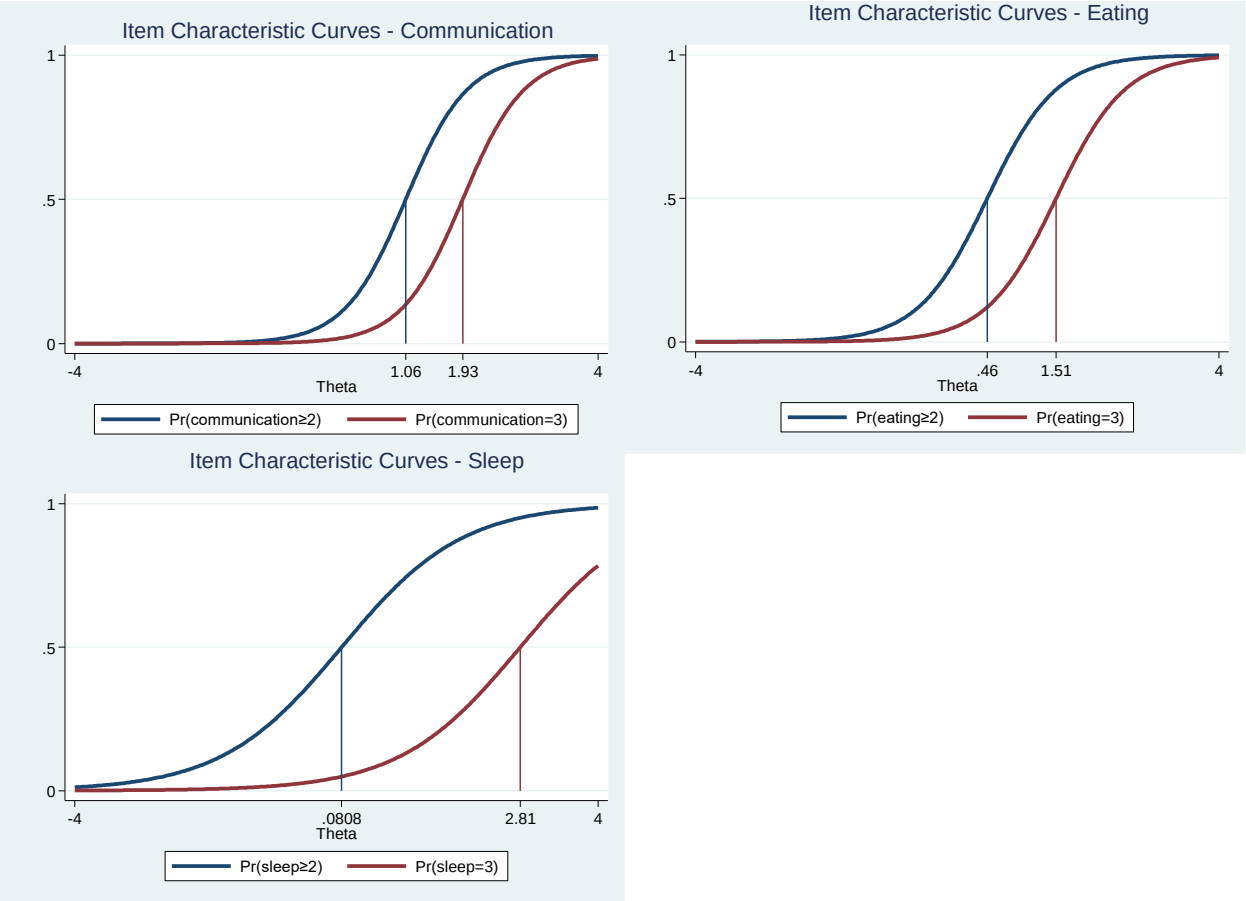


Figure 6-3 Item Characteristic Curves - Alpha Draft

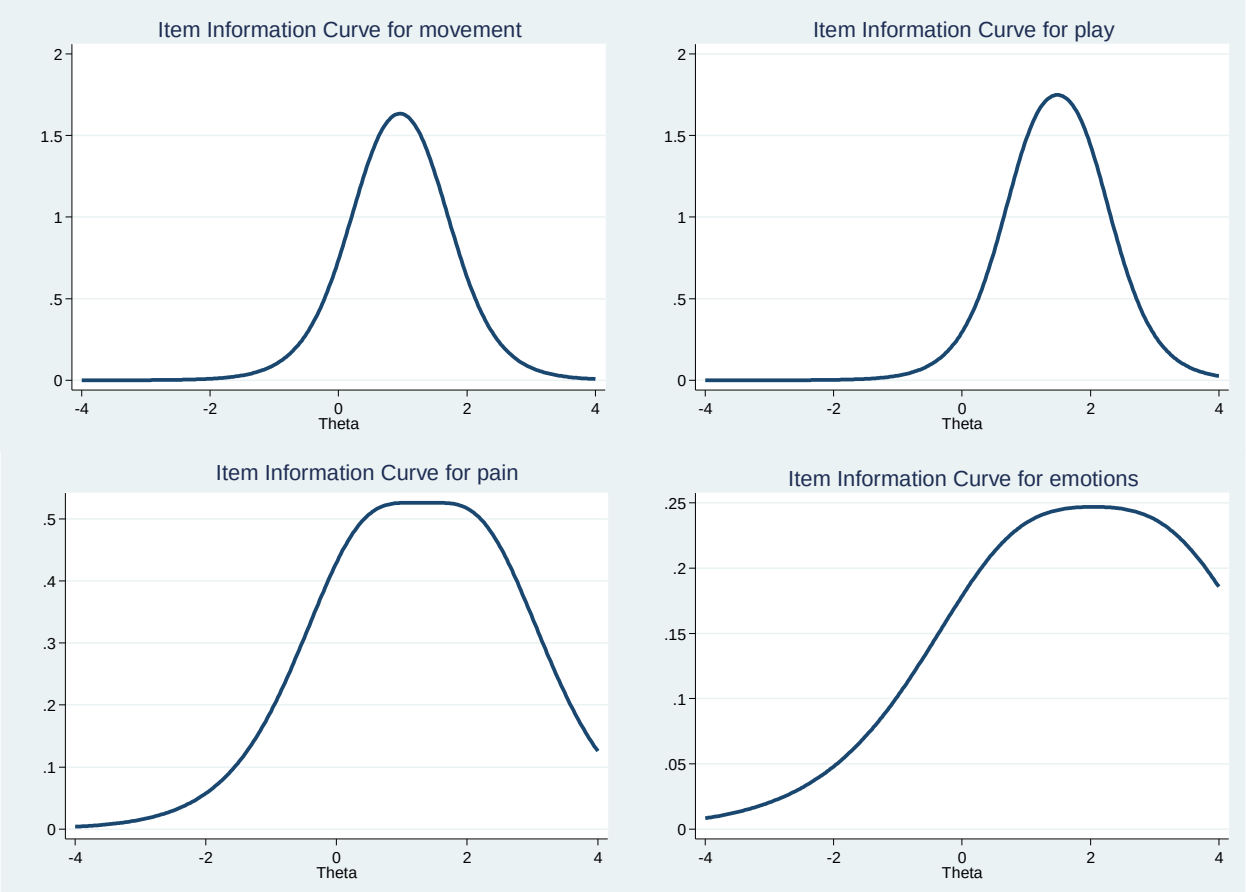
The Item Characteristic Curves for all dimensions show that those who reported no problems and some problems in each of the dimensions had a better HRQoL than those who reported a lot of problems in that dimension (note that theta indicates the degree of problems with HRQoL so higher theta values indicate poorer HRQoL). The item difficulty is related to the theta value for the first transition, from no problems to some problems, and the smaller this value, the less difficult or more commonly reported the next step (some problems) is. It can thus be seen that many respondents reported some problem with sleeping (theta value at 50% probability of moving from no to some problems= 0.0808) compared to the most difficult or most commonly reported some problems was in play (theta=1.19). With regard to discriminating between some and a lot of problems sleep and behaviour demonstrated the greatest change in theta required to move from the one level to the other.

The item discrimination parameter allows for determining how well dimensions identify patients at different levels of the latent trait [287]. A higher discrimination parameter indicates that it is 'easier' to identify a patient at that level. As seen in Table 6-6 below the dimensions of emotions and pain were moderately discriminable as it was difficult to identify patients with no and some problems. Behaviour,

eating and sleeping were poorly discriminable as it was difficult to identify patients with no, some and a lot of problems.

Table 6-6 Item Discriminability on the Alpha Draft

Discriminability	Dimension	Discrimination Parameter for 'no and some problems'	Discrimination Parameter for 'a lot of problems'
High	Movement	4.09	5.22
	Play	5.16	5.22
	Relationships	4.45	4.02
	Communication	4.89	5.24
Moderate	Pain	2.34	4.22
	Emotions	2.58	3.01
Poor	Behaviour	1.88	2.67
	Eating	2.58	4.96
	Sleeping	0.36	3.74



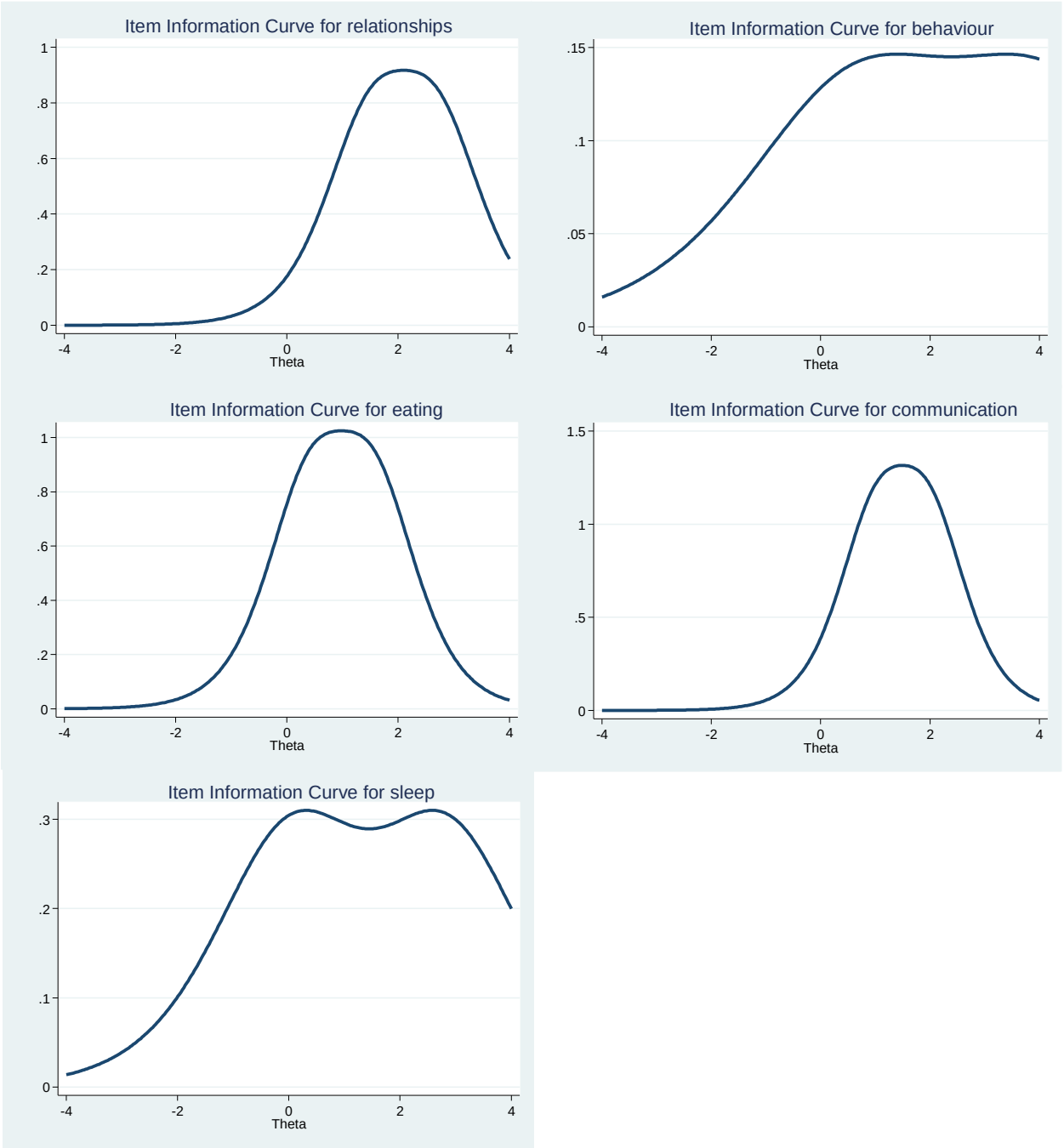
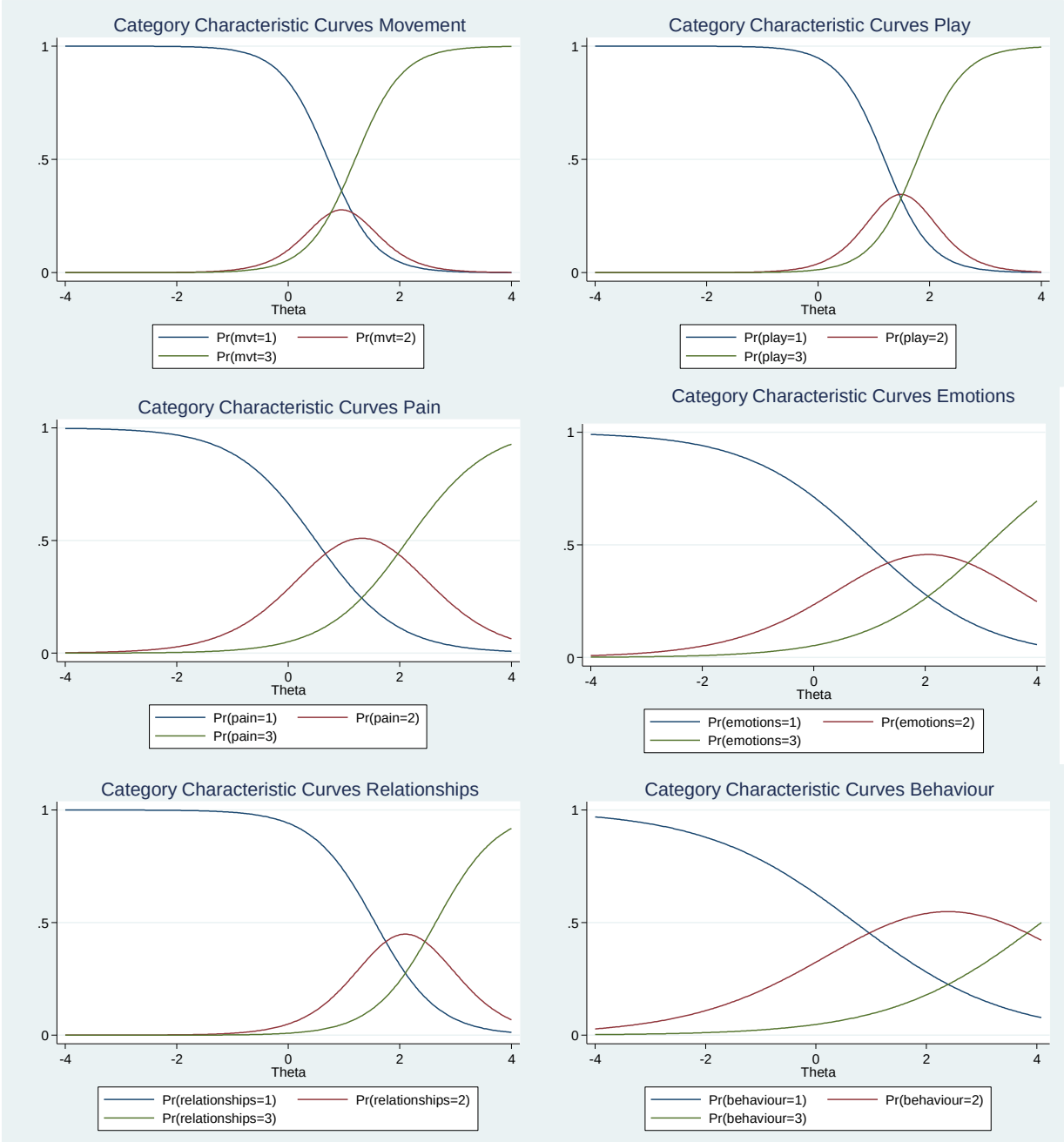


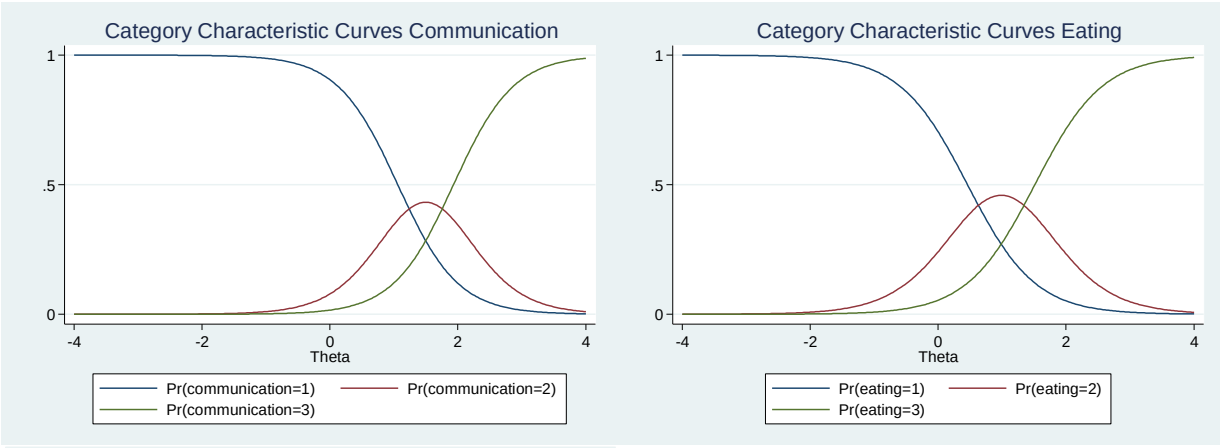
Figure 6-4 Item Information Curves for Dimensions on the Alpha Draft

Movement, play communication and eating are well shaped graphs with slope values above 1 (Figure 6-4). These items provide important information to the scale. Relationships and pain provide slightly less information with the slope value below one but greater than 0, 5. Dimensions of sleep (<0. 3), emotions (<0. 25) and behaviour (<0. 15) provide the least value with slope values <0.5.

Finally, the thresholds at which respondents move from one level to the next was examined. 'Ordered' thresholds are desirable, i.e. the theta value of 50% probability of a respondent being reported to move

from no problems to some problems should be lower than the theta value at which there is a 50% probability that they will move from some to a lot of problems. The results are presented in Figure 6-5 below in the Category Characteristic Curves for each dimension.





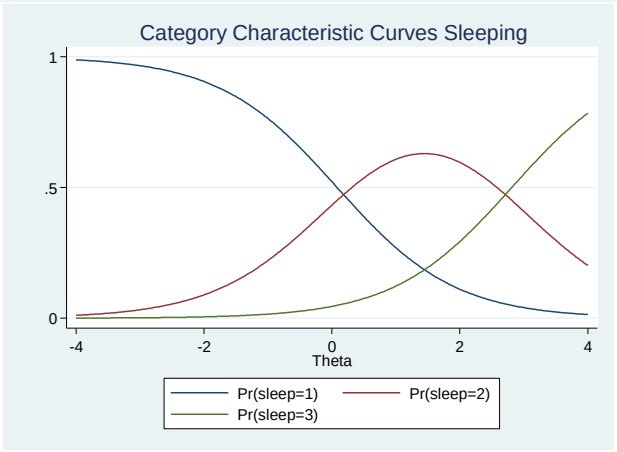


Figure 6-5 Category Characteristic Curves for Dimensions on the Alpha Draft

1 No problems, 2* some problems, 3* A lot of problems*

The thresholds for all dimensions intersect as one would expect except for dimensions of movement and behaviour (Figure 6-5). Movement and behaviour showed similar results with no problems and a lot of problems intersecting at a lower theta than no problems and some problems indicating a disordered threshold.

6.2.3.7 VAS – Alpha Draft

The VAS scores were compared between the two groups of children and were significantly higher for TD than for AI Children (p=0.008). Mean value for TD 86.86 (std dev= 17.23) (IQR 82-91), Mean value for AI=76.9 (std dev=19.80) (IQR 71 -83) T value=2.7.

There was no correlation between age and VAS for AI (r=-0.06, p=0.67) or TD children (r=-0.15, p=0.3).

Multiple regression analysis with the VAS as dependent variable and dummy variables representing the different levels of the accounted for 55% of the variance as seen in Table 6-7 below.

Table 6-7 Regression Analysis of VAS for the Alpha Draft

	b*	Std. Err. Of b*	b	Std. Err. Of b	t(76)	p-value
Intercept			92.8	2.21	42.08	<0.05
Mvt 2*	-0.04	0.08	-2.2	4.37	-0.51	0.613
Mvt 3*	-0.09	0.10	-4.1	4.79	-0.86	0.390
Daily Act 2*	-0.11	0.08	-7.2	5.09	-1.42	0.159
Daily Act 3*	-0.07	0.09	-5.9	7.02	-0.84	0.405
Play 2*	-0.09	0.08	-6	4.87	-1.23	0.221
Pain 2*	-0.20	0.08	-8.2	3.44	-2.39	***0.019***
Pain 3*	-0.52	0.09	-33.7	5.63	-5.99	***<0.001***
Emo 2*	-0.28	0.08	-12.2	3.43	-3.56	***0.001***
Emo 3*	0.09	0.09	6.4	6.10	1.05	0.296
Rel 2*	-0.20	0.09	-11.8	5.08	-2.32	***0.023***
Rel 3*	-0.08	0.09	-8.2	9.32	-0.88	0.380
Beh 2*	0.19	0.08	7.4	3.04	2.42	***0.018***
Beh 3*	0.02	0.08	1.8	5.99	0.30	0.764
Comm 2*	-0.40	0.08	-21.9	4.39	-5.00	***<0.001***
Eat 2*	0.04	0.09	1.8	3.81	0.46	0.644
Eat 3*	0.00	0.10	0.2	5.25	0.04	0.968
Sleep 2*	0.07	0.08	2.7	2.98	0.90	0.371
Sleep 3*	-0.03	0.08	-2.2	5.44	-0.41	0.685

1 No problem; 2* Some problems; 3*A lot of problems Adj R^2=0.55 (n=95)*

Residual Analysis resulted in the exclusion of six outliers which increased the Adjusted R^2=0.42 to Adjusted R^2=0.55 (Table 6-7). The dimensions of movement, daily activities, play, pain, relationships and communication detracted from the VAS score, as to be expected. However, the dimensions of emotions 3*, behaviour 2*, behaviour 3*, eating 2*, eating 3* and sleeping 2* increased the VAS score.

6.2.4 Discussion and Conclusions Regarding the Alpha Draft

The performance of the Alpha Draft was generally encouraging. Most dimensions and the VAS were able to discriminate between known groups. Cronbach's Alpha was good and showed that the questionnaire had internal consistency. However, it was clear that there were dimensions which were not meeting the criteria for inclusion.

Despite all the information available regarding the performance of each dimension in the Alpha testing exercise, it was still not a simple task to choose the dimensions that should be excluded.

The criteria for inclusion were drawn up based on the criteria for dimension reduction discussed in the narrative review under pre-testing of a new instrument (2.3.3.5) (Table 6-8). Psychometric testing included: evaluation of missing data; frequency of response options for each dimension across the population; presence of ceiling or floor effects (dimensions where the responses favour the high or low end of the scale respectively); reliability of the scale as a whole using Cronbach's alpha as well as inter-item correlation and item-total correlation and factor analysis [123], [134]. The dimension were then further examined, in terms of whether they were correctly grouped to measure HRQoL by determining: 1) the equivalence of item variance (by examining the symmetry of the item-response distribution), 2) factor analysis (to ensure that items did not load on multiple factors or that they did not all load on any of the factors) and 3) whether the dimensions showed divergent validity [72], [123], [151], [153], [168], [169]. All of these psychometric properties were weighted equally and dimensions performing poorly across all of these tests were considered for exclusion.

Table 6-8 Criteria Indicating Poor Performance of a Dimension on the Alpha Draft

Criteria	**Mvt**	**Daily Act**	**Play**	**Pain**	**Emo**	**Rel**	**Beh**	**Comm**	**Eat**	**Sleep**
Acceptability		X								
No significant difference between AI &TD							X			
Ceiling Effect in AI		N/A	X		X	X		X		
Floor Effect in AI		N/A								
Increase/ No change to Cronbach's Alpha							X			
Dimension Poorly correlated with scale (Item-rest correlation)							X			X
Factor Analysis		N/A								
Proportion of Problems reported >20% between age groups	X	N/A	X						X	X
Regression Analysis – Increase VAS score					X		X		X	X
ICC – Dimension does not show monoticity (S curve)		N/A								
ICC – Least severe Dimensions		N/A			X		X			
Item Information Curve; Discriminability Slope <0.5		N/A			X		X			X
Disordered Thresholds	X						X			

X indicates that the dimension did not meet the criteria

Dimensions of daily activity, emotions, behaviour and sleep performed poorly across all criteria for dimension exclusion set out in the conceptual framework. Repeated regression analysis was performed excluding dimensions of daily activity, emotions, behaviour and sleep (Table 6-9).

Table 6-9 Regression Analysis with Six Identified Dimensions After Dimensions Reduction on the Alpha Draft

	b*	Std. Err. of b*	b	Std. Err. of b	t(90)	p-value
Intercept			92.4	2.15	43.05	0.000
mvt2*	0.069	0.090	-3.8	4.93	-0.77	0.443
mvt3*	0.059	0.104	-3.1	5.42	-0.57	0.573
play2*	0.092	0.085	-6.1	5.65	-1.08	0.282
pain2*	0.329	0.085	-13.9	3.57	-3.88	***<0.001***
pain3*	0.389	0.086	-26.0	5.77	-4.50	***<0.001***
rel2*	0.086	0.086	-5.2	5.26	-1,00	0,322
rel3*	0,106	0,091	-11,9	10,20	-1,16	0,248
comm2*	0,240	0,088	-13,2	4,83	-2,73	***0,008***
eat2*	0.087	0.099	3.9	4.45	0.88	0.383
eat3*	0.109	0.099	-6.2	5.63	-1.10	0.275

1 No problem in dimension; 2* 2* problems in dimension; 3* A 3* of problems in dimension Adjusted R^2=0.38 (n=101)*

Although the Adjusted R^2=0.38 of the revised model was less, the remaining dimensions, apart from some problems with eating all detracted from HRQoL. Problems with pain and some problems with communicating significantly reduced the VAS (Table 6-9).

6.3 Development and Testing of the Beta Draft

The results from the pre-testing of the Alpha Draft indicated that dimensions of daily activities, behaviour, emotions and sleep needed to be excluded. The dimension of daily activities was excluded as many caregivers reported it as inappropriate and did not subsequently score it for their children. The dimensions of emotions had a ceiling effect, the presence of problems with communication increased the VAS score and IRT analysis showed that it was a less severe dimension with poor discriminability. Results from the dimension of behaviour indicated there was no significant difference between AI and TD children, the removal of the item improved the internal consistency of the scale, the item was further poorly correlated with the scale. Problems reported in the dimension of behaviour increased the VAS sore and IRT scores shoed that the item was less severe, showed poor discriminability and disordered thresholds. The dimension of sleep also performed poorly as it was poorly correlated with the scale, the proportion of problems was greater than 20% between age groups and IRT showed poor discriminability.

Some of the other dimensions were somewhat problematic regarding the proportion of problems which were reported across the age groups. This was of particular note in the dimensions of communication and the more physical dimensions of movement and play where there was greater than 20% difference in the proportion of reported problems between age groups. It was necessary to ascertain whether a single question with detailed descriptors of criterion behaviour for each age, were able to measure HRQoL across the age group from birth to 36 months. These dimensions were both identified as important dimensions for all age groups in both cognitive interviews and the Delphi study and met the other criteria. Thus, it was decided that they should be retained but that the descriptors might need modification.

The description for the dimension of mobility in the Alpha Draft was prescriptive with observable behaviour being referenced for the most notable gross motor milestones. In other words a criterion referenced descriptor was used to describe the typical milestones of a child in this age group e.g. Movement *(0-1 month: grasping, sucking) (2-5 months: plays while on tummy) (6-7 months: sitting) (9-11 months: crawling and standing) (12-36 months: walking)* (Appendix 13). This was referenced similarly for the dimension of communication. The decision was thus made to reword the dimension to ask the caregiver if the dimension was achieved by their child at an age appropriate level, i.e. asking the caregiver to norm reference his/her response e.g. Movement *(moves about at an age appropriate level)* (Appendix 16). All of the dimensions were reworded in this manner except for pain. Results from the cognitive interviews (4.5.1) showed that caregivers of pain or discomfort and worried, sad or unhappy were most often compared to the child's own behaviour than to that of other children. Furthermore, pain performed well across all age groups with

similar proportions of problems reported across the three age groups. Thus the descriptor for pain was retained e.g. Pain *(painful behaviour includes: grimace, restless movement, inconsolable cry)* (Appendix 16).

The Beta Draft was thus constructed with the six dimensions identified from the Alpha Draft. The layout was not changed as this had been well received. The Beta Draft was thus renamed to HRQoL-6D-IT, as it now consisted of six dimensions (Appendix 16).

6.3.1 Aim

Testing of the Beta Draft to determine whether it was necessary to reduce any further dimensions as well as whether the dimensions and wording of the dimensions was appropriate to all children aged 0-36 months.

6.3.2 Objectives

The specific objectives were similar to those of the testing of the Alpha Draft. The objectives related to the dimensions were to determine which dimensions needed to be reduced. This was based on the specific objectives noted. The responsiveness of the dimensions was evaluated by examining the response patterns for floor and ceiling effects. The reliability of the scale and individual dimensions was assessed using Cronbach's Alpha. The dimensions were assessed for their equivalence across the age groups through the proportion of no problems which were reported and the 95% confidence intervals. The structure of the questionnaire was examined using exploratory factor analysis. The structure of the questionnaire was further examined using IRT to determine: individual item severity, dimension monoticity, the usefulness of the information and the order of the thresholds. The dimensions which influence VAS scores were identified through regression analysis.

6.3.3 Methodology

The same methodology was used as in the testing of the Alpha Draft, although there were some differences. As the Alpha Draft had indicated that there was less variance in the responses of the caregivers of TD children, compared to AI children, only the care-givers of children with AI were included. The sample size was reduced to 60 based on the rule of thumb of ten participants per variable (six dimensions) and thus 60 children were recruited [286]. The participants recruited in the testing of the Beta Draft were different to those recruited in the Alpha Draft testing. Caregivers were asked to complete the interviewer administered HRQoL-6D-IT, Beta Draft (Appendix 16).

6.3.4 Results

6.3.4.1 Descriptive Statistics

Table 6-10 Representation of Age Groups Across the Sample for Beta Draft Testing

Age Group (months)	Number
0-12	24
12-24	20
24-36	18
TOTAL	60

The number of children were spread across the age groups with the 0-12 month group having slightly more (24) participants and the 24-36 month age group slightly less (18) (Table 6-10). It is worth noting that six out of the twelve children in the 0-12 month age group were less than one month of age.

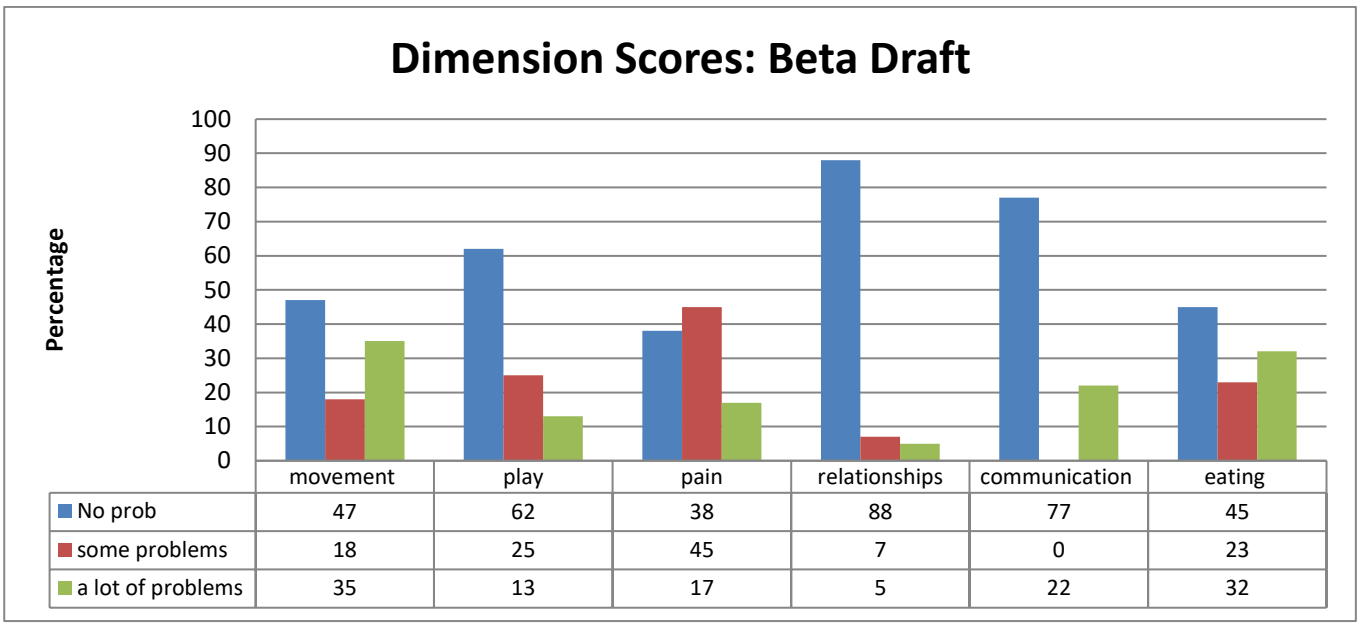
6.3.4.2 Acceptability, Layout and Wording of the Beta Draft

Comments from the interviewer on the acceptability, layout and wording of the Beta Draft

The dimensions on the Beta Draft were acceptable to all caregivers. The six caregivers of children under one month of age struggled to complete all of the dimensions except for the dimension of pain. These difficulties were noted by the researcher collecting the data as caregivers all commented that the questions were difficult to complete as it was not evident to them whether their child was struggling or not. They attributed this to the fact that they felt their child's ability was so minimal in all of the dimensions except pain and eating. Thus these children were all scored as having no problems in the other dimensions. These problems were not reported by any of the caregivers of older children who completed the Beta Draft.

6.3.4.3 *Frequency of Descriptor Responses - Beta Draft*

The percentage of problems reported in each dimension is given in Figure 6-6 below.



	movement	play	pain	relationships	communication	eating
No prob	47	62	38	88	77	45
some problems	18	25	45	7	0	23
a lot of problems	35	13	17	5	22	32

N=60

Figure 6-6 Percentage of Problems Reported in Each Dimension on the Beta Draft

Ceiling effects were shown for relationships (89%) and communication (78%) but the other dimensions demonstrated a spread of responses across the categories (Figure 6-6).

6.3.4.4 *Performance Across the Age Groups – Beta Draft*

In order to examine the equivalence of the responses to each dimension per age group, the proportion of caregivers reporting some or severe problems was calculated (Table 6-11, Figure 6-7).

Table 6-11 Problems Identified per Dimension by Age Group on the Beta Draft

		Movement	Play	Pain	Relationships	Communication	Eating
0-12 months (n=24)	Problems	6	3	15	1	2	8
	No problems	16	19	7	21	20	14
	Proportion with problems	0.27	0.14	0.68	0.05	0.09	0.36
	CI	0.13	0.05	0.47	0.01	0.03	0.20
		0.48	0.33	0.84	0.22	0.28	0.57
1-12 months (n=16)	Problems	6	3	11	1	2	5
	No problems	10	13	5	15	14	11
	Proportion with problems	0.38	0.19	0.69	0.06	0.13	0.32
	CI	0.18	0.07	0.44	0.01	0.04	0.14
		0.61	0.43	0.86	0.28	0.36	0.56
12-24 months (n=20)	Problems	15	9	13	4	4	13
	No problems	5	11	7	16	16	7
	Proportion with problems	0.75	0.45	0.65	0.20	0.20	0.65
	CI	0.53	0.26	0.43	0.08	0.08	0.43
		0.89	0.66	0.82	0.42	0.42	0.82
24-36 months (n=18)	Problems	11	11	9	2	7	12
	No problems	7	7	9	16	11	6
	Proportion with problems	0.61	0.61	0.5	0.11	0.39	0.67
	CI	0.39	0.39	0.29	0.03	0.20	0.44
		0.80	0.80	0.71	0.33	0.61	0.84

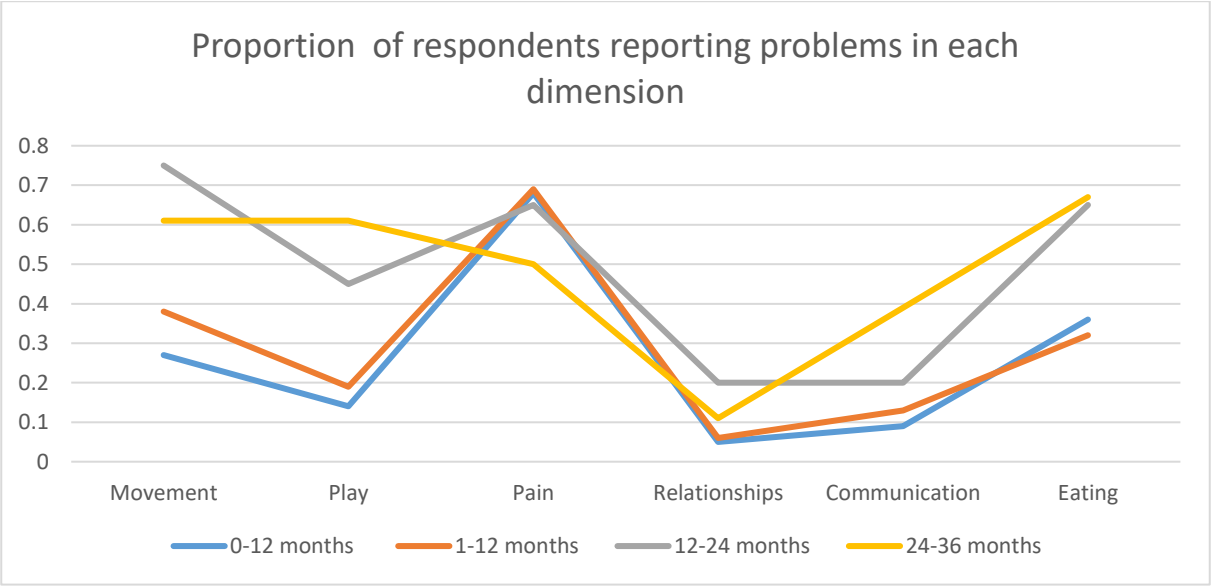


Figure 6-7: Proportion of Respondents Reporting Problems in Each Dimension per Age Category – Beta Draft

Removing the children aged <1 month marginally improved the distribution of proportion of problems across the age groups for the dimensions of play and communication (Table 6-11). Although the absolute proportions are different with non-overlapping CIs in many instances between the age groups, the pattern of responses are similar in terms of which dimensions were reported to have the greatest proportion of problems (Figure 6-7).

6.3.4.5 Reliability, Internal Consistency and Factor Structure - Beta Draft

Reliability of the measure as a whole was good with α=0.73 (Table 6-12) [176]. The reliability of the measure as a whole would however increase if pain (0.77) or eating were removed (0.76). Item-rest correlations show how the dimension is correlated with the measure if calculated from the other five dimensions. Dimensions which were not well correlated with the measure as a whole included pain (0.19) and eating (0.29). This is similar to the results found in the factor analysis in Table 6-13 below where pain and eating are identified as a separate factor.

Table 6-12 Internal Consistency and Reliability: Cronbach's Alpha - Beta Draft

N=60	**Item-test correlation**	**Item-rest Correlation**	**Alpha if item is removed**
Movement	0.76	0.58	0.66
Play	0.78	0.66	0.65
Pain	0.41	0.19	0.77
Relationships	0.68	0.57	0.69
Communication	0.81	0.67	0.63
Eating	0.54	0.29	0.76
Alpha of the Questionnaire			**0.73**

Table 6-13 Factor Analysis (Varimax Normalized) Beta Draft

N=60	**Factor 1**	**Factor 2**
Movement	0.77	0.14
Play	0.84	0.11
Pain	-0.01	0.84
Relationships	0.77	0.09
Communication	0.90	0.07
Eating	0.20	0.71
Explained Variance	2.74	1.25
Proportional Total	0.46	0.21

Value	**Eigenvalue**	**% Total variance**	**Cumulative Eigenvalue**	**Cumulative %**
Factor 1	2.87	47.88	2.87	47.88
Factor 2	1.11	18.56	3.99	66.44

There were two factors which emerged (Table 6-13). The 1st factor accounted for 47.88% of the variance of the scale and included dimensions related to activities and participation. The second factor accounted for 18.55% of the variance and included pain and eating, which can both be considered body functions. The combination of the two factors accounted for 66.44% of the total variance of the measure.

6.3.4.6 *Item Response Theory (IRT) Analysis – Beta Draft*

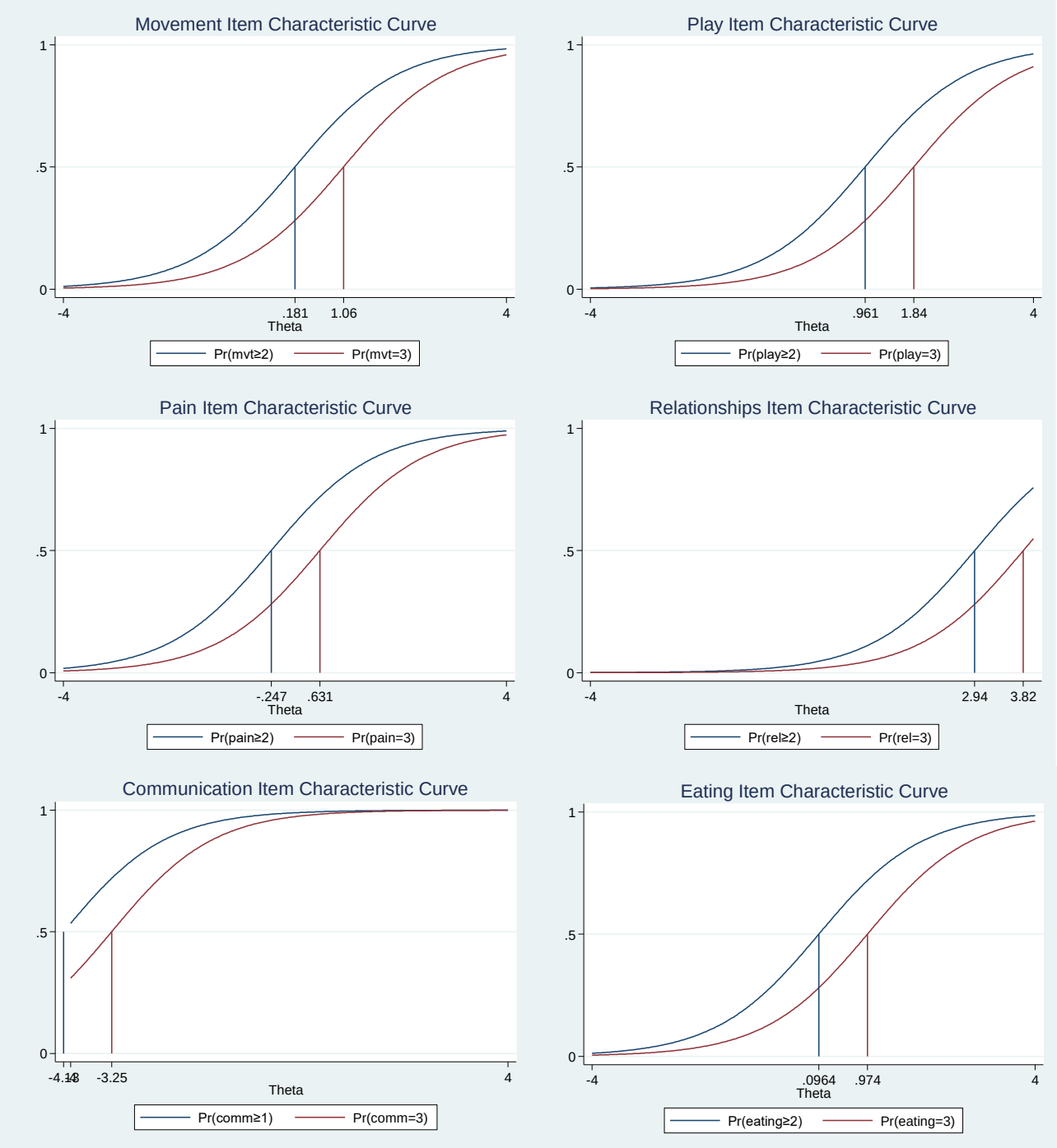


Figure 6-8 Item Characteristic Curve - Beta Draft

The Item Characteristic Curves demonstrates an 'S-curve' for the probability and thus these dimensions demonstrate monotonicity in all dimensions, apart from communication (Figure 6-8). This could be attributed to the fact that most children scored no problem with communication (78%), no children scored some problems with communication and a few children scored a lot of problems with communication (22%) (Table 6-11). The difference between the theta value with a 50% probability of moving from no to

some problems and that of moving from some to lots of problems is approximately 0.9 on all dimensions, in other words, a subject will have to improve 0.8 on the theta scale to move from the second to the third level.

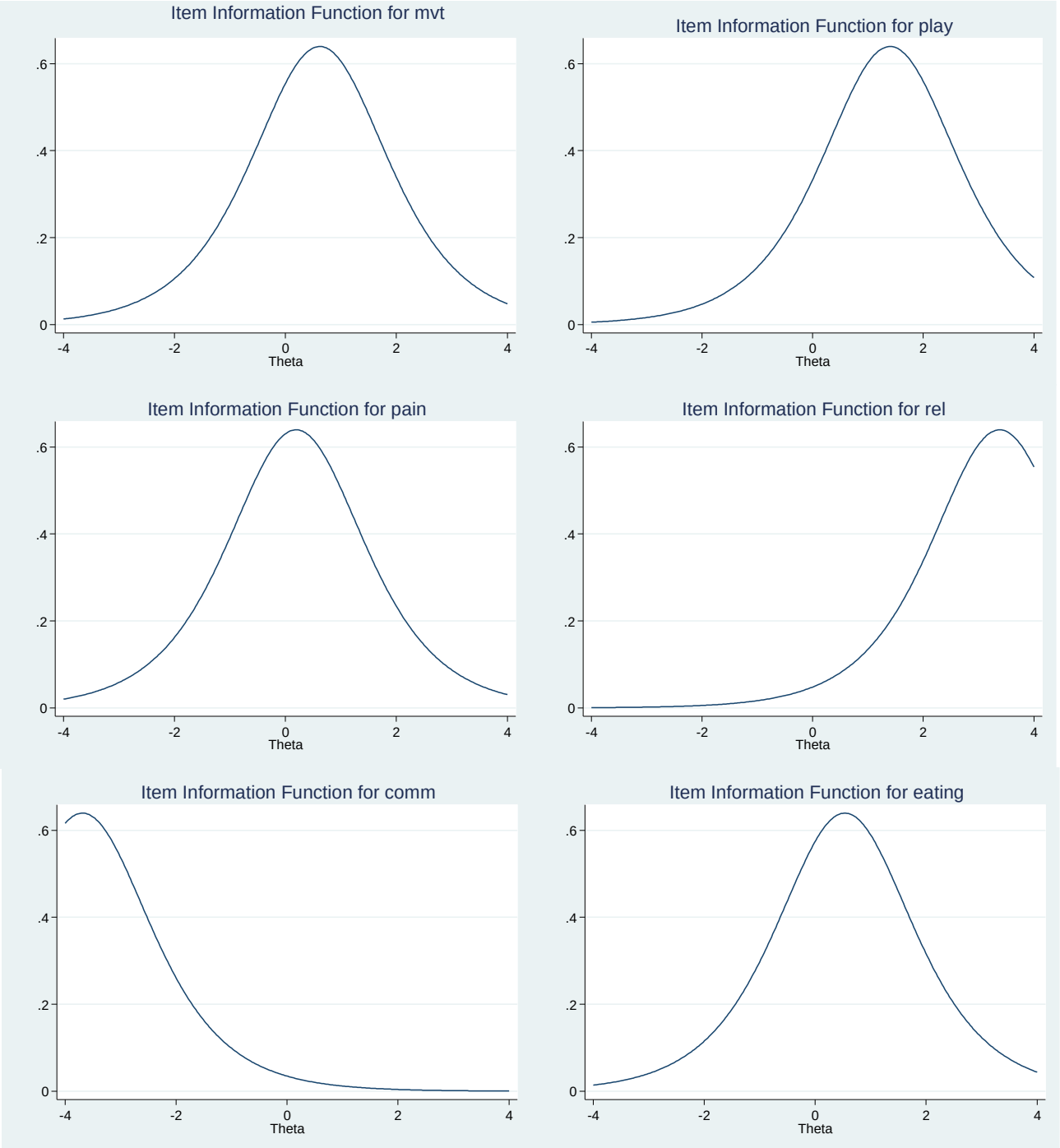
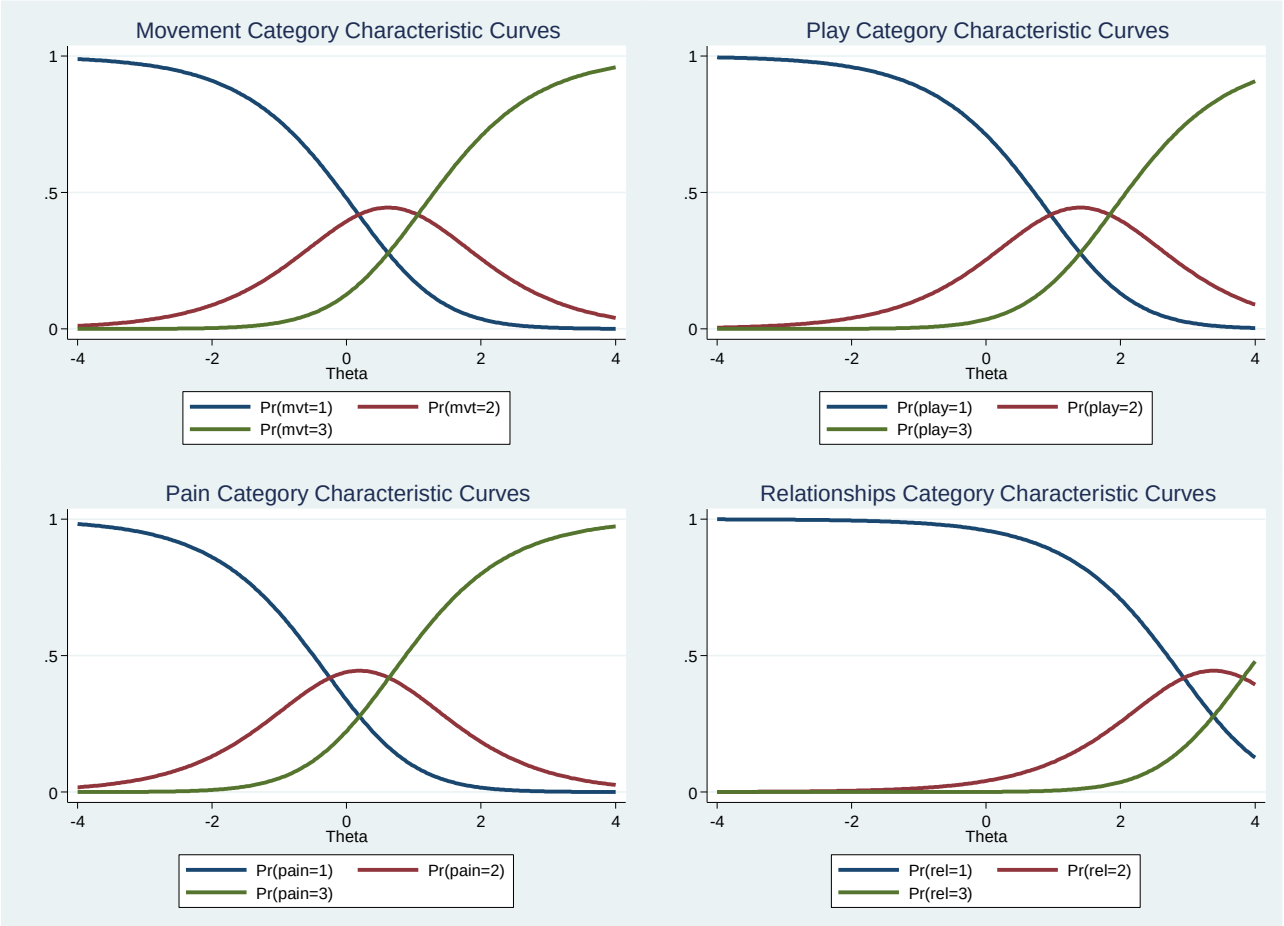


Figure 6-9 Item Information Curves for the Beta Draft

All of the dimensions provide moderate information to the measure with slope value below 1 but >0.5 (Figure 6-9).

The rephrasing of the descriptors resulted in ordered thresholds for five of the dimensions, in other words the point at which the probability of moving from some to lots of problems at 50% was at a higher value of theta, which represents decreasing HRQoL than that of moving from no to some problems (Figure 6-10). Communication was again aberrant as the probability curves for no problems and some problems with communication do not cross. This is attributed to the fact that no child scored some problems with communication. The curve of communication is situated to the left of the graph with a very low theta (reduced HRQoL) due to the fact that no children scored some problems with communication. The curve of relationships is situated to the right of the graph with a high theta due to the fact that a lot of children scored problems with relationships. The level descriptors were therefor appropriate and improved since the Alpha Draft.



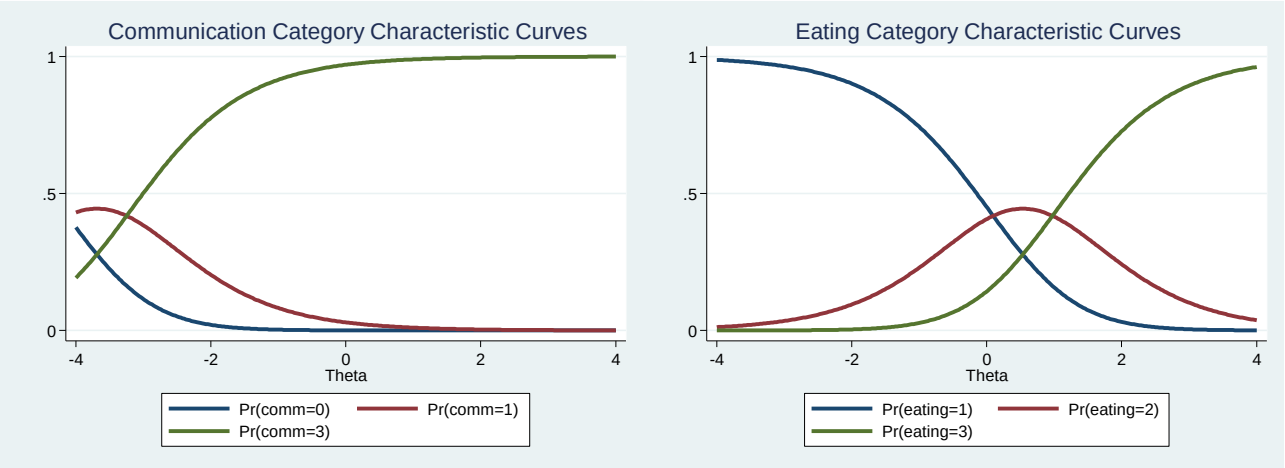


Figure 6-10 Character Characteristic Curves Showing Order of Thresholds for the Beta Draft

1 No problems, 2* Some Problems, 3* A lot of Problems*

6.3.4.7 VAS – Beta Draft

Multiple regression analysis with the VAS as dependent variable and dummy variables representing the different levels of the dimensions resulted in a rather poor fit and only accounted for 19% of the variance. The Communication 2* (some problems) was excluded due to nobody scoring the dimension. The model improved when infants less than one month of age were excluded and accounted for 26% of the variance, once one outlier had been removed (Table 6-14).

Table 6-14 Regression Analysis for Children Aged 1-36 Months

	b*	Std. Err. of b*	b	Std. Err. of b	t(41)	p-value
Intercept			85.24	5.17	16.50	0.05
mvt 2*	-0.14	0.16	-6.98	7.52	-0.93	0.358
mvt 3*	-0.18	0.17	-7.26	7.01	-1.04	0.306
play 2*	-0.28	0.16	-12.39	7.06	-1.75	0.087
play 3*	-0.18	0.18	-10.02	9.81	-1.02	0.313
pain 2*	-0.08	0.14	-3.19	5.58	-0.57	0.570
pain 3*	-0.15	0.15	-7.79	7.39	-1.05	0.299
rel 2*	-0.15	0.16	-11.05	11.76	-0.94	0.353
rel 3*	-0.25	0.15	-20.86	12.55	-1.66	0.104
comm 3*	0.04	0.21	1.99	9.67	0.21	0.838
eating 2*	-0.20	0.15	-9.32	6.97	-1.34	0.188
eating 3*	-0.10	0.15	-4.26	6.23	-0.68	0.498

1 No problem, 2* some problems, 3* a lot of problems (n=53)*

Although no coefficients were significant, they were all in the right direction and detracted from VAS except for comm 3* which added to VAS. This implies that the dimensions included on the descriptive system are related to the general health of the child. Thus if there is a problem in one or more of the dimensions it detracts from the child's perceived general health. This relationship strengthens the content validity of the dimension inclusion and re-affirms that they are representative of the definition of health.

6.4 Discussion

The draft questionnaires were tested to establish the dimensions which should be included in the final questionnaire. The criteria for inclusion included whether the dimension contributed to a good overall questionnaire structure, whether the dimensions were equivalent across the age groups, whether the levels of report were ordered and whether the dimensions were sensitive enough to pick up problems. From testing of the Alpha Draft with 101 caregivers of AI and TD children it was clear from the results of the psychometric testing that some of the dimensions needed to be removed.

- The dimension of helping with daily activities was removed as it was rated as not applicable by 56% of the caregivers and was not included in subsequent analysis due to the high number of 'missing values' (Table 6-2).
- The dimension of controlling emotions was removed due to the fact that it was found to have a ceiling effect in AI children (Table 6-2). Report of a lot of problems increased the VAS score (Table 6-7) this could be attributed to the fact that children's emotions were more labile and the reporting of problems in this dimension was not seen as a concern with their general health but rather an expectation for the age of the child. The dimension was one of the least severe and showed poor discriminability between levels of report (Figure 6-5). The severity and discriminability of the dimension was attributed to the high number of children reporting a lot of problems with the dimension.
- The dimension of behaviour had seemed like a good candidate but was removed as it was the only dimension which was not associated with the presence of acute illness. As seen in Table 6-2 there was a significant association between the numbers of problems and presence of acute illness or TD in all dimensions apart from behaviour. TD and AI children had the same number of caregivers reporting a lot of problems with behaviour (Table 6-2) suggesting that a problem with behaviour is prevalent among all children and not necessarily as a result of illness or a change in health. Removal of the dimension improved the internal consistency and reliability of the questionnaire (Table 6-4). Some problems with the dimension significantly increased the VAS score (Table 6-7) which could be a due similar reasoning given for the dimension of emotions. A problem with behaviour was prevalent among all children and could be considered a normal aspect of

development rather than an attribute to health. IRT analysis showed that it was one of the lease severe dimensions, with poor discriminability (Figure 6-3) and the thresholds between level reporting were disordered (Figure 6-5). The results from the IRT analysis could be attributed to the fact that problems with behaviour were a commonly reported problem across AI and TD children (Table 6-2).

- The dimension of sleep was removed as removal of the dimension improved the internal consistency and reliability of the questionnaire the proportion of problems reported in sleeping was much higher in the 0-24 month age group than for the 24-36 month age group, the reporting of problems for sleeping increased the VAS score (Table 6-7) and IRT analysis showed that the dimensions had poor discriminability (Figure 6-3). The poor discriminability of the dimension was similarly attributed to the fact that it was a commonly occurring problem with high report of problems by both AI and TD children (Table 6-2). The dimensions that were selected for removal were not all from one factor and thus did not contribute unique data compared to the other dimensions (Table 6-5). Furthermore, the remaining dimensions represented dimensions of the ICF: body structure and function, activities and participation.

After the removal of these dimensions the structure of the questionnaire was still concerning. The proportion of caregivers reporting problems for the dimensions of play, movement, communication and eating had an incremental decrease across the ages with concern that the single dimensions could in fact not accurately measure problems across the ages (Figure 6-2). This would imply having different descriptors or different sets of dimensions for different ages. The 95% confidence intervals overlapped but there was concern that these bands were large due to the relatively small sample size. The other concern was that the thresholds of the levels of report for the dimension of movement were disordered (Figure 6-10). One of the possible reasons for these results could have been attributed to the descriptions given to each of the dimensions, which were prescriptive (Appendix 13). Results from the cognitive interviews revealed that 48% of the caregivers compared their child to other children of a similar age in the answering of questions for the dimensions of Mob, SC and UA (Table 4-5). Thus, the decision was made to change the wording of the dimensions to include ‘at an age-appropriate level’ or ‘in an age-appropriate manner’ in the Beta Draft (Appendix 16) for further testing. The wording of the pain dimension was kept the same due to the fact that caregivers rarely compared their children to others when completing the dimension of pain (Table 4-6) and that dimension of pain performed well with no obvious change in reporting of problems across the age groups (Figure 6-2).

The Beta Draft was tested on 60 caregivers of AI children only. This decision was made as previous data showed that the measure was most sensitive to AI children. The questions which needed to be answered

with the testing of the Beta Draft was whether or not the structure of the questionnaire was better, whether the dimensions were: sensitive enough to detect problems, equivalent across the ages and if the levels of report were ordered.

The analysis showed ceiling effects for relationships and communication (Figure 6-6). Factor analysis revealed that the scale was multi-dimensional with the emergence of two factors with eating and pain in the second factor (Table 6-13). The internal consistency and reliability of the scale was good and showed that eating and pain gave different information than the other dimensions which is in keeping with the two factors which emerged (Table 6-12). Determining whether the dimensions were equivalent across the age groups proved problematic. The dimensions of movement, relationships and eating all revealed a spike in the proportion of problems reported in the 12-24 month age group (Figure 6-7). One of the considerations was that the medical conditions which affect children at different ages are different and might thus have different consequences. It might have been that respondents did understand what was being asked as there was internal consistency and thus if they were reported as having problems with one dimension they were likely to be reported as having a problem in other dimensions. Unfortunately no data on the medical condition of the children was collected and this could not be verified. The 95% confidence intervals for the dimensions of play, relationships and communication did not overlap across the age groups. The data was analysed again excluding the children younger than one month of age as this was thought to be skewing the reporting of problems in the younger age group. This did yield slightly better results with the 95% confidence intervals of the play dimension overlapping for all age groups and the 95% confidence intervals of the 1-12 and 12-24 month age groups for the dimension of communication overlapped. The discriminability of the communication dimension was poor which could be attributed to the fact that no one was scored as having some problems with the dimensions (Figure 6-6). The discriminability of the eating dimension was also poor which was attributed to the fact that more children were scored as having a lot of problems than some problems with the dimension. Improvement from the Alpha Draft were that the levels of report were ordered for all of the dimensions and although there was a spike in the proportion of reporting of problems in some of the dimensions the problem with an incremental decrease across the age groups was no longer seen. The reporting of problems for all dimensions detracted from the VAS score except for a lot of problems with communication which minimally increased the VAS scores (Table 6-14). The results of both the proportion of reporting problems and regression analysis of the VAS score improved with excluding children under the age of one month.

The dimension of communication performed poorly as it was not sensitive enough to detect some problems and it was not equivalent across the ages. There was however, internal consistency on the Beta Draft with the inclusion of communication and it may have been that the condition of children did not

warrant the selection of some problems. This was however not tested. The dimension of communication further performed well in the Alpha Draft. The decision was made to retain the dimension of communication for further testing on a larger sample on the Delta Draft.

6.5 Conclusion

The reduction of the dimensions from the Alpha Draft as well as the re-wording of the dimensions improved the results attained on the Beta Draft (Table 6-15). The Beta Draft was shown to be multi-dimensional with two distinct factors. It had good internal consistency and reliability. The thresholds for reporting between no problems and some problems and between some problems and a lot of problems were all ordered and the dimensions had better discrimination between levels of report in that a child with problems would be more likely be reported as having problems across the board. The difference between the proportions of problems at different ages would need to be tested in a larger sample to determine whether the reliability and validity increased with the youngest age groups and if a single measure could in fact be used across the age groups. The dimensions performed better when children under the age of one month were excluded and thus the Delta Draft will only be tested for validity and reliability in children aged 1-36 months. It is proposed that pre-mature infants and neonates may need a different measure as the problems which they encounter are different to infants over one month of age.

Table 6-15 Summary of Candidate Items

Review of Generic HRQoL measures	**Cognitive interviews**	**Delphi Study**	**Delphi Round 1**	**Delphi Round 2**	**Alpha Draft**	**Beta Draft**
Walking/ Ambulation	Walking	Walking	Walking			
Mobility	Movement	Movement	Movement	Movement	Movement	Movement
Physical function						
	Upper Limb Movement	Upper Limb Movement	Upper Limb Movement			
	Kicking	Kicking				
	Crawling					
	Achievement of Milestones	Achievement of Milestones	Achievement of Milestones			
Family Activities						
Family Cohesion						
Social						

Review of Generic HRQoL measures	**Cognitive interviews**	**Delphi Study**	**Delphi Round 1**	**Delphi Round 2**	**Alpha Draft**	**Beta Draft**
Relationships		Relationships	Relationships	Relationships	Relationships	Relationships
Doing things with family or friends	Socializing	Socializing	Socializing	Socializing		
Usual Activities	Usual Activities	Usual Activities	Usual Activities			
Washing	Washing	Washing				
Dressing	Dressing	Dressing				
Hobbies	Hobbies	Hobbies				
Sport						
Play	Play	Play	Play	Play	Play	Play
School	School	Pre-School				
	Learning	Learning	Learning			
	School Performance					
Cognition	Cognition	Cognition	Cognition			
	Perception					
Mental Health						
	Motivation	Motivation				
	Attitude					
Emotion	Emotion	Emotion				
Behaviour		Behaviour	Behaviour	Behaviour	Behaviour	
Worried	Worried	Worried	Worried			
Sad	Sad	Sad	Sad			
Unhappy	Unhappy	Unhappy	Unhappy			
	Routine	Routine	Routine			
Self-care		Self-care				
Independence	Independence	Independence	Independence	Independence	Assisting with Daily Activities	
	Dependence on Care	Dependence on Care				
Sleeping	Sleeping	Sleeping	Sleeping	Sleeping	Sleeping	
Eating	Eating	Eating (able to take food orally)	Eating (able to take food orally)	Eating (able to take food orally)	Eating	Eating

Review of Generic HRQoL measures	**Cognitive interviews**	**Delphi Study**	**Delphi Round 1**	**Delphi Round 2**	**Alpha Draft**	**Beta Draft**
	Feeding	Feeding (Ability of child to feed him/herself)	Feeding (Ability of child to feed him/herself)			
	Growth	Growth	Growth			
Toileting	Toileting	Toileting				
Pain	Pain	Pain	Pain	Pain	Pain	Pain
Discomfort	Discomfort	Discomfort	Discomfort			
Mood		Mood	Mood	Mood	Controlling Emotions	
Energy		Energy	Energy			
Self-Esteem	Self-Esteem					
General Health						
	TB Status					
	HIV Status					
	Sickness	Sickness	Sickness	Sickness	VAS	VAS
	Immunizations	Immunizations				
Dexterity	Dexterity	Dexterity				
Senses	Senses	Senses	Senses			
Communication	Communication	Communication	Communication	Communication	Communication	Communication
Environment	Supportive Environment					
Religion	Spirituality	Religion				
	Trust					
	Attitude					
	Hygiene	Hygiene				
	Pride	Pride				
		Crying	Crying			
	Burden of Care					
	Following Rules					

7 Chapter 7: Validity and Reliability Testing of the Delta Draft

7.1 Introduction

A rigorous process of item identification and pruning resulted in a six dimension questionnaire intended to be used from the age of 1-36 months. The next stage was to establish the validity and reliability of the Delta Draft of this new measure, the HRQoL-6D- IT.

7.2 Aim and Objectives

The aim of this chapter was to examine the validity and reliability of the newly developed Delta Draft (HRQOL-6D-IT for children 1-36 months of age (Appendix 20).

The specific objectives of this chapter were, in a group of AI and TD children to establish:

- The concurrent validity of the different dimensions:
  - The pain dimension would be examined by comparing results attained from the FLACC pain scale (children 2-36 months) and the Neonatal Infant Pain Scale (NIPS) (children 1-2 months).
  - The dimension of eating was examined by comparing results attained to a self-designed diet history questionnaire.
  - Movement, play, relationships and communication were compared to corresponding items of the Ages and Stages Questionnaire (Third Edition) (ASQ).
- The discriminant validity of the HRQoL-6D-IT tested by comparing results between known groups: AI, CI and TD.
- The reliability and internal consistency by calculating Cronbach's Alpha and test-retest reliability and the correlation of the dimension scores on a sample of TD children.
- Whether the HRQoL-6D-IT was feasible and by calculating the percentage of missing values and inappropriate responses in both the dimensions as well as the VAS.
- Whether the HRQoL-6D-IT was responsive by examining the response patterns of each of the dimensions for floor and ceiling effects.
- Known group validity between VAS scores of AI, CI and TD children.
- VAS scores were not affected by the age of the child.
- Item response characteristics such as the discriminability, thresholds and information functions of the each dimension.

- Whether the six dimensions were significant predictors of the VAS scores was identified through regression analysis.
- Finally to explore the relationship between the child's HRQoL and the caregiver's scores on the EQ-5D-3L through regression analysis and comparison of their VAS scores.

7.3 Methodology

7.3.1 Research Design

A descriptive, analytical, cross-sectional study design was utilised to determine the reliability, validity and feasibility of the Delta Draft. The HRQoL-6D-IT was developed as a proto-type instrument in English and thus tested on caregivers who were literate in English only. The previous measures in this study were administered during an interview or with interviewer stand-by assistance. Due to the fact that this is a self-report measure it was send home to caregivers of TD children to self-complete. The researchers contact details were provided if any clarity was needed. For caregivers of AI and CI children the researcher explained the purpose of the study took informed consent and was available if any clarity was needed. As the items on the final draft of the questionnaire were the same as the Beta Draft no data on the perception of the items was needed.

7.3.2 Study Setting

The proposed research settings included a tertiary level paediatric hospital, situated in Cape Town, managing both AI children and those suffering from chronic conditions (CI). The hospital treats over 250 000 patients a year in both the acute and chronic services. Three open day care centres in Port Elizabeth accepting children from 1 – 5 years of age participated in the study. Three toddler play groups, two in Port Elizabeth and one in Cape Town, comprising of children of all ages (with no lower age limit) were included in the study.

7.3.3 Participants

The participants for this study included the caregivers of AI and CI children from a population of in-patients and out-patients respectively at a children's hospital; caregivers of TD children from a population of children attending three open English day care centres as well as toddler play groups.

7.3.3.1 Inclusion Criteria

Caregivers of children aged between 1-36 months accessing acute or chronic health care services or attending any of the participating day-care centres or toddlers groups were included. The caregiver of the child was defined as any person over the age of 18, who lived with the child and was wholly or partly responsible for the care of the child's physical and emotional needs e.g. mother, father, aunt, uncle, grandparent, brother or sister.

7.3.3.2 Exclusion Criteria

Caregivers who were unable to read or write English were excluded as the HRQoL-6D-IT was an English proto-type instrument and the validity and reliability needed to be tested before translation into other languages. Caregivers of children who were medically unstable, terminally ill, or who were born prematurely and had not yet reached the corrected age of one month were excluded. An unstable child was classified as any child who was less than 24 hours post admission to ICU, less than 24 hours post-surgery or any child who has had any acute changes in their medical condition.

7.3.4 Sample Size Determination

Sample size calculation proved to be challenging as there was no one objective which we aimed to test. The HRQoL-6D-IT consists of six equally important dimensions and a general rating of health on the VAS scale. It was thus decided to calculate the sample size on a number of the set objectives and make the decision based on the highest number of participants needed in each group to satisfy all of the statistical tests.

If one considered the reliability of the scale and what the resultant effect would be on the overall reliability of the scale if a dimension was removed it was decided to consider the sample size based on Cronbach's Alpha. It had been shown that the coefficient alpha was not only dependent on the sample size but also on the largest eigenvalue of the sample data set. According to Yurdugül (2008), if one set the first eigenvalue between 3.00 and 6.00 the minimum sample size of n=100 was sufficient for an unbiased estimator of the coefficient alpha [285].

When analysing factor analysis based on the correlation matrix of the variables a large sample is usually needed. It was suggested, as a rule of thumb, that at minimum of ten observations was needed per variable [286]. Considering that there were six dimensions one would need a minimum of 60 (6 x10)

participants per group. The study aimed to compare three groups of children (AI, CI and TD) thus a minimum sample of 180 participants was needed.

If one considered the discriminant validity between TD, CI and AI children in order to determine the sample size, VAS was used as an objective measure. It was expected that the central limit theorem would apply and that the one-way ANOVA would be used to compare the perceived rating of health (VAS scores) between groups. The calculation was done in Statistica version 13 and was based on RMSSE of 0.47 which was calculated based on the expected difference in VAS of 15 between the groups, with a standard deviation of 15 for three groups, with a Type 1 Error Rate of 0.05 (Table 7-1). The reference values were from a South African study using the EQ-5D-Y [221]. A minimum of 36 children per group was required to ensure a power of 95% for a one-way ANOVA.

Table 7-1 Sample Size Calculation Difference in VAS Scores ANOVA, 1-Way Fixed Effects

Number of Groups	3
RMSSE	0.47
Noncentrality Parameter (Delta)	4.47
Type I Error Rate (Alpha)	0.05
Power Goal	0.95
Actual Power for Required N	0.95
Required Sample Size (N) per group	**36**

The level of agreement between dimensions of the HRQoL-6D-IT and corresponding scores of the ASQ, NIPS or FLACC pain scale and the self-designed diet history questionnaire was calculated using the Kappa co-efficient. The scores on the ASQ, NIPS, FLACC and diet history questionnaire were converted to categorical data representing a lot of problems, some problems and no problems on the questionnaire or dimension. The kappa sample size was calculated backwards to ensure that the sample size of 60 using the rule of thumb was in fact large enough [288]. If one considered the sample size of 60 per group suggested by the rule of thumb the null value of kappa (0.6), power (80%) and kappa to detect statistical significance (0.9) were all sufficient (Table 7-2) [288], [289].

Table 7-2 Sample Size Calculation of Kappa

Null value of kappa	0.6
Power	80%
Kappa to detect statistical significance from the null value	0.9
Expected proportion of positive ratings	0.5
Expected sample size (N) per group	**56**

In order to determine the minimum sample size needed for the TD children for test-retest a sample size calculation based on an Intraclass Correlation Coefficient (ICC) with an expected co-efficient of 0.6 was calculated using GPower version 3.1. The type 1 error (α) was set at 0.05 and the Type II error rate (β) was set at 0.02. The sample size of 19 was computed (Table 7-3). The same calculation was repeated using a Pearson's Correlation with an expected co-efficient of 0.6 and the same sample size was computed (Table 7-3). Thus only 19 participants will be required to complete the second administration of the HRQoL-6D-IT.

Table 7-3 Test-Retest Sample Size Calculation Based on ICC and Pearson's Correlation

Type I Error Rate (Alpha)	0.05
Type II Error Rate (Beta)	0.2
Correlation Co-efficient	0.6
Expected Pearson correlation (r)	0.6
Required Sample Size (N)	**19**

7.3.5 Instrumentation

Each of the dimensions of the HRQoL-6D- IT needed to be validated against an accepted, reliable and validated measure. All of the instruments needed to be scored via observational methods as participants were completing the HRQoL-6D- IT which was based on observable behaviour, as recommended by the FDA proxy-report guidelines [13], [33]. Due to the fact that the EQ-5D-Y proxy was not validated in this young age group and it did not perform well in the cognitive interviews it was not included in this study to determine convergent validity. The outcome measures were completed by caregivers thus measures requiring additional training were not considered.

7.3.5.1 The Ages and Stages Questionnaire (Third Edition) (ASQ)

The ASQ is a caregiver-completed questionnaire to monitor development in children aged one month to five years of age [290], [291]. There are 21 age specific questionnaires each comprising of 30 developmental items which are categorized into five different domains namely: communication, gross motor, fine motor, problem solving and personal social (Appendix 21) [290], [291]. The questions are comprehensive with a reading level ranging between fourth to sixth grade [290]. The ASQ domains assess the developmental capability of the child and has three scoring levels for each item: yes, sometimes and not yet [290]. As the ASQ is a screening tool it comprises of a simple scoring sheet where yes, sometimes and not yet are awarded ten, five and zero points respectively. The total score of 60 for each domain has two cut-off points which categorises domain scores as: the development of the child appears on par with developmental norms; the development of the child is below the cut-off for normal development and needs to be monitored and the development of the child needs to be assessed by a professional for appropriate treatment [290], [291].

The ASQ domain scores of communication, gross motor and personal social were compared to corresponding HRQoL-6D-IT dimension scores of communication, movement and relationships. The combined scores of ASQ domains of fine motor and problem solving were compared to the HRQoL-6D-IT dimension of play. The ASQ domain scores were re-scored according to the average cut-off scores observed for children aged 2-36 months to match the scoring style of the HRQoL-6D-IT (Table 7-4).

Table 7-4 ASQ Score Conversion to an Equivalent Level on the HRQoL-6D-IT

Average cut-off points on the ASQ domains	**Equivalent level on the HRQoL-6D-IT**
0-15 (on par with developmental norms)	1 (no problems)
20-30 (development needs to be monitored)	2 (some problems)
35-60 (development needs to be assessed by a professional for appropriate treatment)	3 (a lot of problems)

The ASQ has been found to be valid and reliable internationally [290], [292]–[294]. Furthermore, the ASQ has been implemented successfully in both health care settings as well as population screening programmes [290], [292]–[295]. The ASQ research kit further has reporting sheets and recommended activity sheets (per age group) which can be sent out to caregivers [290]. The reporting sheets were adapted for the purpose of the study to be distributed to caregivers of TD children participating in the study (Appendix 22) together with a suggested sheet of activities which they could enjoy with their child (regardless of their developmental capabilities) (Appendix 23).

7.3.5.2 FLACC Pain Scale

For children who are not able to subjectively rate their pain, due to lack of cognitive and verbal skills, observation of pain behaviour is a validated approach of assessing pain [232]. The FLACC Scale (Appendix 24) is an observational behaviour tool which has been validated in children from two months to seven years and is used widely in the clinical setting [232], [233], [296]–[299]. The scale considers typical pain behaviour in the face, legs, arms, activity, crying and consolability and scores each item from 0-2, a cumulative score out of ten gives an indication of pain behaviour [232], [233], [296]–[299]. A score of zero indicates no pain, a score 1-3 indicates mild discomfort or pain, a score of 4-6 indicates moderate discomfort or pain and a score of 7-10 indicates severe discomfort or pain [233], [296]–[298]. Due to the rating of the scale being divided into categories of no pain, mild and moderate pain and severe pain it was decided that these scores would be converted to the same scale of the HRQoL-6D-IT as seen in Table 7-5 below.

Table 7-5 FLACC Score Conversion to an Equivalent Level on the HRQoL-6D-IT

FLACC Scale score	**Equivalent level on the HRQoL-6D-IT**
0 (no pain)	1 (no pain)
1-3 (mild pain) 4-6 (moderate pain)	2 (some pain)
7-10 (severe pain)	3 (a lot of pain)

7.3.5.3 Neonatal Infant Pain Scale (NIPS)

Due to the fact that the FLACC scale was only valid for children aged two months to seven years an additional pain scale for children aged one to two months needed to be included. Pain scales such as the Premature Infant Pain Profile (PIPP) and the Neonatal Postoperative Pain Assessment Score (CRIES) (for Crying, Requires oxygen to maintain saturation >95 percent, Increased vital signs, Expression, and Sleeplessness) used to measure pain in neonates relied on observational and physiological changes [300], [301]. The Neonatal Infant Pain Scale (NIPS) was one of the only pain scale which relies solely on observational measure and did not require any additional training to complete [300]–[302]. The NIPS was a measure scoring behaviour on observation of the neonates facial expression, cry, breathing pattern, activity in their arms and legs, and their state of arousal (Appendix 25) [300]–[302]. These observations were similar to those scored on the FLACC pain scale for children aged from two months. Each of these behaviours on the NIPS was scored from zero to one, except for the presence of cry which was scored from zero to two [300]. A total score of zero indicated no pain, a score of 1-3 indicates mild pain and a score of

4-7 indicated severe pain. Due to the rating of the scale being divided into categories it was converted to the same scale of the HRQoL-6D-IT in a similar manner to the FLACC scale (Table 7-6).

Table 7-6 NIPS Conversion to an Equivalent Level on the HRQoL-6D-IT

NIPS score	**Equivalent level on the HRQoL-6D-IT**
0 (no pain)	1 (no pain)
1-3 (mild to moderate pain)	2 (some pain)
4-7 (severe pain)	3 (a lot of pain)

7.3.5.4 Self-Designed Dietary Information Questionnaire

A literature search of dietary and eating assessment tools revealed three main instruments used in children: dietary record, 24 hour dietary recall and food-frequency questionnaire [303]–[305]. In the case of very young children all of the information was gathered from the caregiver or someone who was with the child for most of the day [304], [305]. The dietary record required respondents to record everything that they had eaten and drunk as well as the brand of food, recipe, cooking methods and portion sizes (generally immediately after it was consumed) for a specified time period (usually two to three days) [303]–[305]. The 24 hour dietary recall was an interview conducted by a trained interviewer asking the respondent to report everything which they (or their child) had eaten or drunk in the past 24 hours [303]–[305]. The food frequency questionnaire was a comprehensive pre-determined list of food items which the respondents were asked to report the frequency of each food item consumed over a specified period (anywhere between eight and 36 days) [303]–[305]. Brief food frequency questionnaires had been developed for children to make completion easier [306]–[309]. These assessment methods had high respondent burden and the 24 hour dietary recall required training of an interviewer [304], [305]. The assessment tools available were complex in nature and care needed to be taken to ensure that the measure used recorded issues relating to eating rather than the families food security.

Thus due to the lack of an assessment tool evaluating eating in general as opposed to nutritional status the decision was made to design a questionnaire. The aim of the questionnaire was to assess general constructs of eating and drinking which may be affected due to health across the age range of 2-36 months. Due to the fact that the HRQoL-6D-IT is assessing the dimensions of health for 'today', the same time period was used for the questionnaire (Appendix 26). The questionnaire was kept short and simple for the self-completion by caregivers. The questions were related to the amount of nutrition they were receiving orally in terms of: whether they were bringing up any of their food or milk, if they were eating or drinking as much as usual, the same amount as other children their age and at regular time intervals. Their ability to

feed orally in relation to their competence with chewing/sucking and swallowing, gagging on food and tiring during eating was also assessed. Due to the fact that the HRQoL-6D-IT dimension of eating specifies 'adequate oral intake to sustain growth an age appropriate level' (Appendix 26) eating orally was differentiated by asking whether an alternative feeding route via gastrostomy or intravenous infusion was used. The items were scored according to a self-designed scoring system with a higher score indicating a better eating ability. The questionnaire was pre-tested by an independent researcher to approve the content, structure and comprehension of questions. Necessary changes were made according to the input received. The scores from the self-designed instrument were categorised according to the levels of report on the HRQoL-6D-IT (Table 7-7).

Table 7-7 Dietary Information Score Conversion to an Equivalent Level on the HRQoL-6D-IT

Dietary Information Score	**Equivalent level on the HRQoL-6D-IT**
7-8 (good eating ability)	1 (no problems)
4-6 (moderate eating ability)	2 (some problems)
1-3 (poor eating ability)	3 (a lot of problems)

7.3.5.5 EQ-5D-3L

It has been proposed that a child's health is influenced by that of the caregiver due to their close proximity, interaction and subsequent moulding of development [310]–[318]. Many studies have found that maternal depression influences the child in terms of their cognitive and emotional development [311]–[318]. Furthermore children born to HIV positive mothers have been found to have delayed development [310]. There is an interest to note whether these influences are similar when assessing the HRQoL of the child, especially if reported by proxy. This could identify future research as well as provide a basis for the recommendation of measurement of child HRQoL by proxy with or without taking into account the caregivers HRQoL.

The caregivers HRQoL was measured using the EQ-5D-3L an adult self-report measure assessing five dimensions of health: mobility (Mob), self-care (SC), usual activities (UA), pain/discomfort (PD), anxiety/depression (A/D) and a general rating of health status on a VAS [106], [219] (Appendix 27). Each of the dimensions of health had three levels of report: no problems, some problems or moderate and unable/extreme or confined to bed [106], [219]. The VAS asked the respondent to rate their health status on a scale from 0 (worst imaginable health status) to 100 (best imaginable health status) [106], [219]. All ratings are made by the respondent based on their health of 'today' [106], [219]. The EQ-5D has been used

in South Africa across health conditions as well as cultural and language groups [221], [238], [319]–[321]. The dimension scores and the VAS score were used compared to the dimension and VAS scores of the children as well as against the contextual factors.

7.3.5.6 Contextual Information

Contextual information needed to be gathered about both child and caregiver to ascertain whether their HRQoL scores were influenced by factors related to their health or external factors. The general information form was self-designed in order to capture the information relevant to the study (Appendix 19). The questionnaire was pre-tested by an independent researcher to approve the content, structure and comprehension of questions. Necessary changes were made according to the input received. The form included the name of the child which allowed the researcher an opportunity to identify the child and discuss the results with the caregiver if anything of concern was noted. Information about the child's age and sex and the relationship of the caregiver to the child was collected for descriptive analysis. It was hypothesised that neither the child's age nor gender would affect the results as was shown with the TAPQoL [322]. This was however in contrast to results found using the Kidscreen [323] and EQ-5D-Y [221] in older children where girls where girls were found to have more variation in their scores than boys and the HRQoL of children worsened with the increase in age[323] [221]. Details regarding the child's medical condition, medication and any event(s) which upset them in the last week were recorded to study their influence on the child and caregivers HRQoL [248]. The child's medical condition and medication may explain variations in the results obtained for individuals or groups of children. An event which upset the child or caregiver in the last week was left open to interpretation by the caregiver. If the caregiver reported an event they were asked to clarify what that event was. Although experiencing an upsetting event did not appear to influence the HRQoL in older children on the EQ-5D-Y [248], the relationship with younger children needed further clarity. The experience of an upsetting event may further explain a deviation in a child or caregiver's HRQoL from other children or caregivers in that disease group. Caregiver and child information with regard to the area in which they lived was recorded in order to calculate the Living Standard Measure (LSM) of the family to determine if it had an influence on either the child or the caregivers HRQoL. Family wealth was found to predict HRQoL scores on all KIDSCREEN dimensions [324]. Unfortunately The South African Audience Research Foundation (SAARF) who collects the data only had data for the Cape Town Metropolitan in three districts (North, South West and South East) and only one value for the entire Port Elizabeth and Uitenhage district [325]. Thus, the analysis was not subsequently carried out. The caregiver's medical condition and any event(s) which upset them in the last week were recorded to study their influence on both the child and caregivers HRQoL.

7.3.6 Procedure

After ethical approval was obtained from the UCT HREC (HREC/REF: 336/2014) (Appendix 2), permission from the children's hospital (Appendix 14) and day-care centres the HRQoL-6D- IT was tested for reliability and validity. All of the caregivers of children attending the day-care centres and play groups were sent a detailed description of the study before the study commenced (Appendix 28). As pre-arranged with each of the day-care centres and play groups a research pack was delivered for each child under the age of 36 months. The research packs were all collated in the same order and stapled in the top left hand corner. The research pack consisted of detailed information regarding the study and informed consent (Appendix 19), a form capturing general information about the caregiver and child (Appendix 19), HRQoL-6D-IT the proxy report form to capture the child's HRQoL (Appendix 20), ASQ Parent Report Form to assess the child's development (Appendix 21), FLACC an observational pain scale (for children aged 2-36 months) (Appendix 24) or the NIPS an observational pain scale for neonates (for children aged one to two months) (Appendix 25), Dietary Information Questionnaire to assess the eating habits of the child (Appendix 26) and the EQ-5D-3L caregiver self-report HRQoL Questionnaire (Appendix 27). The HRQoL-6D-IT was the first outcome measure to be completed as it was the outcome measure which was subject to testing and this ensured that the other, more detailed, outcome measures did not influence the reporting of the HRQoL-6D-IT. The order of the other measures was standardised according to the order of the dimensions on the HRQoL-6D-IT. The EQ-5D-3L was placed last in the research pack as it was not related to the main outcome of establishing validity and reliability for the HRQoL-6D-IT. These research packs (which were individualised for each child according to their age) was placed in an envelope (with the child's name on it) and put in the child's school bag or handed to the caregiver when they collected their child at school. The caregivers who consented to participate were requested to return the envelope, sealed, with the completed research pack therein after a period of three days. All of the research packs which were returned were analysed by the researcher and the results of the ASQ were used to compile a report of the child's development according to the caregivers answers (Appendix 22). The child's ability was categorised similarly to the scoring sheet of the ASQ as: above average, performed well or needs attention. If any of the TD children scored low enough in any of the domains to 'need attention' the caregiver was contacted telephonically to discuss their child's development or to set up a meeting to discuss their child's development. Referral to the appropriate health practitioner was made following the consultation with the caregiver. The day after the caregivers returned the research packs the completed report (Appendix 22) and a list of recommended activities (Appendix 23) was sent to each of the caregivers of TD children in a sealed envelope together with an information page (Appendix 29) and a second copy of the HRQoL-6D-IT to complete. The caregivers were requested to complete the second HRQoL-6D-IT measure and return it to school in the sealed envelope after one week. The period of one week was the most convenient collection time for the schools. Marx et al (2003) showed

that there was no statistically significant difference in test-retest reliability between measures taken two days or two weeks apart [326] . Thus the time period of one week was agreed upon. Only caregivers of children attending day care centres were asked to participate in the completion of a second copy of the HRQoL-6D-IT as the play-groups did not meet regularly.

Caregivers of AI children were recruited from the in-patient wards of a children's hospital. The recruitment process was done systematically throughout the hospital. Participants were first recruited in the B1 and then B2 medical ward from the first cubicle to the last cubicle in numerical order in each of the wards. The subsequent wards were done in the same manner from the first to the fourth floor of the hospital. The pattern was repeated until 80 caregivers had consented and participated in the study. The caregivers were given detailed information regarding the study and informed consent (Appendix 18) was taken, 24 hours or later, post admission to the acute hospital. With the assistance of the researcher caregivers were asked to complete the research packs which were ordered in the same way as described above. If children were noted to have developmental concerns during the completion of the research pack, the caregivers were asked if their children were being assessed or treated by any of the allied health professionals. If the children had not been assessed or treated with the caregiver's permission they were referred to the appropriate health professional. The study was limited to English, as this is a proto-type instrument which needs to be developed and validated in a source language, English, before translation into other languages.

Caregivers of CI children were recruited from the waiting rooms of specialist clinics at the children's hospital. These clinics included: neurology, cardiology, oncology, haematology, allergology, respiratory, rheumatology, developmental services and physiotherapy. Caregivers were approached from their position in the room; the caregiver closest to the left hand side of the door was recruited first and in a clockwise direction thereafter. After those caregivers were invited to participate, any new caregivers were approached in the order that they entered the waiting room. The caregivers were given detailed information regarding the study and informed consent (Appendix 18) was taken. With the assistance of the researcher, caregivers were asked to complete the research packs which were ordered in the same way as described above. If children were noted to have developmental concerns during the completion of the research pack, the caregivers were asked if their children were being assessed or treated by any of the allied health professionals. If the children had not been assessed or treated with the caregiver's permission they were referred to the appropriate health professional.

7.3.7 Data Management

The information from the Contextual Information, HRQoL-6D- IT, ASQ, FLACC, Dietary History and EQ-5D-3L was entered into an Excel spread sheet under the code allocated to each individual. The information was stored in a secure office at the children's hospital and in locked cupboards at the respective day care centres. The researcher and the research supervisors had access to the raw data as well as the analysed data. No identifying information was recorded on the Excel spreadsheet or for any other analysis.

Age range of the children for inclusion was 1- 36 months. To ensure that the instrument was applicable to children across this age band, three age groups were assessed during data analysis. The age groups were divided as follows: one month 0 days – 11 months 30 days (1-12 months); 12 months 0 days – 23 months 30 days (12-24 months) and 24 months 0 days - 35 months 30 days (24-36 months).

Descriptive analysis to determine frequency of problems, acceptability, and responsiveness was done on SPSS version 23. Reliability and Factor Analysis was performed in Statistica version 13. Vassarstats (http://vassarstats.net/) was used to calculate Fisher Exact scores, probability scores and 95% confidence intervals. Small Stata version 14 was used for IRT analysis.

7.3.8 Statistical Methods

Statistical analysis was conducted using Statistica Version 13. Frequency (ordinal data), median (ordinal and categorical data), range and mode (categorical data), were used to describe the data. The Shapiro-Wilk Test (numerical data from the VAS) and the Kolmogorov-Smirnov test (ordinal data) tested the normality of the data. Non-parametric tests (median and Spearman's rank correlation) were utilised for ordinal and non-normally distributed data. Parametric tests (mean, standard deviation and Pearson's correlation co-efficient) were utilised for normally distributed numerical data. The Chi-square scores were calculated to determine significance between dimension scores of AI, CI and TD children and across age groups. The distribution of frequency of dimension scores across condition groups was used to determine the responsiveness of the dimensions in terms of ceiling and floor effects. The dimensions were assessed for their equivalence across the age groups through the proportion of no problems which were reported and the 95% confidence intervals. Rotated Factor Analysis was used to examine the structure of the questionnaire and determine the variance each of the factors contributed to the scale. The structure of the questionnaire was further examined using IRT to determine: individual item severity, item monoticity, the usefulness of the information and the order of the thresholds. The construct validity of the HRQoL-6D- IT dimensions and the associated domain scores on the ASQ, FLACC scale or NIPS and Dietary Information was

calculated by Kappa. The known group validity was established from the significance of chi-square results of dimension scores across AI, CI and TD children and one-way ANOVA of the VAS scores between AI, CI and TD children. Post Hoc Analysis was used to identify VAS means for AI, CI and TD children, which were different from each other. Reliability and internal consistency of the HRQoL-6D-IT and dimensions was established through Cronbach's Alpha. Test-retest reliability of the HRQOL-6D-IT was calculated on the correlation of dimension scores according to Pearson's Correlation. Regression Analysis of the VAS scores was used to determine the effect that the dimension scores, contextual factors and the mothers health and HRQoL had on the VAS. The level of statistical significance was set at $p \leq 0.05$.

7.3.9 Ethical Consideration

Ethical principles of autonomy, confidentiality, beneficence/non-maleficence and justice applied in the testing of the Delta Draft are detailed below and were based on the Helsinki Declaration [243].

Autonomy

Prior to commencement of the study, consent was obtained from the children's hospital where the study was to take place (Appendix 14). All participants who met the inclusion and exclusion criteria were given an information pack which detailed the purpose of the study, their role in the study, the risks and benefits, the confidentiality of their information and their right to refuse to partake in the study or withdraw at any point (Appendix 18). This information was further explained by the researcher, if any clarification was needed. Thereafter informed consent (Appendix 18) was obtained from each of the participants who had given consent of their own free will.

Confidentiality

The confidentiality of each participant was maintained by keeping the information in a secure locked cupboard and their names were deleted during the data analysis process. The electronic files were password protected on a secure computer. No participants were identified in the analysis or write-up of the research.

Beneficence and non-maleficence

The data collection did not affect the medical treatment which the child received or the way in which the caregivers were perceived at the health institution. The participants did not incur any costs for their involvement in the study and thus no monetary re-imbursement was given. There were no known risks to the participants and therefore no insurance was required for research-related injuries. The research had a potential to develop a new HRQoL measure, for very young children, which would be valid and reliable for

use in children in South Africa. This would have had future benefit in measuring the HRQoL of very young children. This could have assisted in improved understanding of the child's health condition and could improve management thereof.

If any developmental or maladaptive behaviour concern were noted the caregiver of that child was consulted and with their consent referral to the relevant practitioner was made. Two AI children were referred for a physiotherapy assessment, with caregiver consent, based on their answers to the ASQ and one caregiver, with consent, was referred to the social worker for social support based on her discussion around the data collection. Based on the ASQ data, six TD children were noted to have concerns with their development. Each of the caregivers was contacted per telephone to discuss or set up an appointment to discuss their child's development. After consultation with the TD caregivers one of the children was referred to an educational psychologist for assessment, one of the children was referred to an occupational therapist for assessment and the mother was advised to monitor the child's speech development, two of the children were referred to a speech therapist with consideration for referral to an occupational therapist, the other two caregivers opted to monitor their children's development before referral for further assessment.

If any signs of neglect or abuse were noted referral to the necessary authority would have been made, in line with legal requirements. One caregiver confided in the researcher that her and her child had been subject to abuse, the researcher confirmed with the caregiver that a case of abuse had been opened with the South African Police Services and a restraining order was granted against the perpetrator. The family were in the care of the community social worker.

Justice

Every caregiver who was eligible to participate in the study was recruited. Caregivers across a range of socio-economic backgrounds were recruited and no-one who met the entrance criteria was excluded on the grounds of ethnic group, gender preference, religion or any other reason.

Due to the fact that a proto-type English version of the measure was being developed only English speaking caregivers were recruited. This limited the eligibility of a great number of the caregivers AI and CI children as the majority of caregivers utilising the hospital's service were Afrikaans or Xhosa speaking.

7.4 Results

7.4.1 Demographic and Medical Data

Caregivers of TD children were recruited from day-care centres and play groups in Port Elizabeth and Cape Town. Research packs were sent to 112 caregivers inviting them to participate in the study. Caregivers of 67 children consented and returned the research packs. A second copy of the HRQoL-6D-IT was sent to 46 of the TD children attending day-care centres. The number of repeat measure of the HRQoL-6D-IT returned amounted to 23.

All of the caregivers of AI children who were approached and met the inclusion and exclusion criteria consented to participate in the study. All 60 of the caregivers of AI children completed the study. All of the caregivers of CI children who were approached and met the inclusion and exclusion criteria consented to participate in the study. All 60 of the caregivers of CI children completed the study.

Table 7-8 Number of Children and Age Range of Children per Condition Group

Age Group (months)	AI	CI	TD	TOTAL
1-12	38	14	6	58
12-24	12	23	20	55
24-36	10	23	41	74
TOTAL	60	60	67	

Chi-sq= 51.88 (p<0.001)

As seen in Table 7-8 there were a higher number of TD children as more research packs were sent out due to the uncertainty of the completion rate, all the data returned were included for analysis. The Chi-square test indicated that the percentage in each condition group differed by age group and that age group was not independent of condition ($p<0.001$)." There were a higher number of children in the 1-12 month category for AI children than CI or TD. There were a higher number of children in the 24-36 month category in the TD group than the AI or CI group.

The Chi-Squared test indicated that the percentage in each condition group did not differ by gender (Chi-sq-4.34; p=0.114) and gender was independent of condition group although there were double the number of males to females in the CI group (Table 7-9).

Table 7-9 Gender of Children per Condition Group

	AI	CI	TD	Total
Female	31	20	31	82
Male	29	40	36	105

Chi-sq= 4.34 (p=0.114) (n=187)

Table 7-10 Diagnosis of Children per Condition Group

Primary Diagnosis or Reason for Hospitalization	Secondary Diagnosis	AI (n=60)	CI (n=60)	TD (n=67)	Total (n=187)
None			1	58	59
Developmental Delay			6		6
Allergy			1	1	2
Asthma		1		1	2
Breath holding spells				1	1
Bronchiolitis Obliterans		1	1		1
Cerebral Palsy Total			**18**	**1**	19
	RVD+		*2*		
	Epilepsy		*5*		
Congenital Heart Disease Total		**8**	**1**		9
	Downs Syndrome	*1*			
	Cerebral Palsy & TB		*1*		
	Other Genetic Syndrome	*1*			
Disseminated TB		1			1
Diarrheal disease Total		**6**		**1**	7
	Cerebral Palsy & Epilepsy	*1*			
Down's Syndrome			1		1
Eczema			2		2
Epilepsy Total			**6**		6
	Genetic Syndrome		*1*		
	RVD+		*1*		
Eczema			2		2
Foetal Alcohol Syndrome				1	1
General Surgery		10			10
GIT		3	2		5
Haematology			5		5
Kidney Failure					1
Liver Disease Total		**4**			4
	RVD+	*1*			1
Liver Transplant			2		2

Neurology		2	2		4
Neurosurgery		5			5
Oncology			5		5
Orthopaedic Surgery			1		1
Pneumonia Total		**11**		**1**	12
	Congenital Heart Disease	*2*			
	Downs Syndrome	*1*			
	RVD+	*1*			
Sever Acute Malnutrition		1	1		2
TB Meningitis		1			1
Throat Infection				1	1
Upper Airway Obstruction with Tracheostomy Total		**6**	**3**		9
	Genetic Syndrome	*4*	*1*		
	Epilepsy	*1*			
	Neurosurgery		*1*		
	Genetic Syndrome, Congenital Heart Disease & Epilepsy	*1*			
Totals		60	60	67	

(n= 187)

Secondary conditions are calculated with the total score of the primary diagnosis or reason for admission, but frequencies of secondary conditions are still noted per condition group in italics

As seen in Table 7-10 most of the TD children did not have any medical diagnosis, but there were TD children who suffered from asthma, allergies, breathe holding spells, cerebral palsy (hemiplegia), diarrheal disease, pneumonia and a throat infection. The majority of AI children had undergone general surgery and a number of children had multiple health conditions but the highest number of primary reasons for hospitalisation included: pneumonia, congenital heart disease, upper airway obstruction, neurosurgery intervention and diarrheal disease. The aetiologies for the CI children were also complex but include: cerebral palsy, developmental delay, epilepsy, haematology, oncology, and children with an upper airway obstruction requiring a tracheostomy.

Table 7-11 Diagnosis of Children Across Age Groups

Primary Diagnosis or Reason for Hospitalization	**Secondary Diagnosis**	**1-12 Months (n=58)**	**12-24 Months (n=55)**	**24-30 Months (n=74)**	**Total (n=187)**
None		4	18	37	59
Developmental Delay		1	4	1	6
Allergy			1	1	2
Asthma				2	2
Breath holding spells				1	1
Bronchiolitis Obliterans			1	1	1
Cerebral Palsy Total		**5**	**8**	**6**	19

	HIV		*2*		
	Epilepsy		*4*	*1*	
Congenital Heart Disease Total		**7**	**1**	**1**	9
	Downs Syndrome	*5*			
	Cerebral Palsy & TB	*1*			
	Other Genetic Syndrome	*1*			
Disseminated TB				1	1
Diarrheal disease Total		**5**		**2**	7
	Cerebral Palsy & Epilepsy			*1*	
Down's Syndrome		1			1
Eczema		1		1	2
Epilepsy Total		**1**	**4**	**1**	6
	Genetic Syndrome	*1*			
	HIV			*1*	
Eczema			1	1	2
Foetal Alcohol Syndrome				1	1
General Surgery		7	1	2	10
GIT		2	2	1	5
Haematology			1	4	5
Kidney Failure			1		1
Liver Disease Total			**1**	**3**	4
	HIV			*1*	
Liver Transplant			2		2
Neurology		2	2		4
Neurosurgery		2	2	1	5
Oncology		1	2	2	5
Orthopaedic Surgery				1	1
Pneumonia Total		10	2		12
	Congenital Heart Disease	*2*			
	Downs Syndrome		*1*		
	HIV	*1*			
Severe Acute Malnutrition		*2*			2
TB Meningitis		1			1
Throat Infection				1	1
Upper Airway Obstruction with Tracheostomy Total		**6**	**1**	**2**	**9**
	Genetic Syndrome	*3*	*1*		
	Epilepsy	*1*			
	Neurosurgery	*1*			
	Genetic Syndrome, Congenital Heart Disease & Epilepsy	*1*			
Total		58	55	74	187

(N=187)

Secondary conditions are calculated with the total score of the primary diagnosis or reason for admission, but frequencies of secondary conditions are still noted per age group in italics

The greatest number of children with cerebral palsy, developmental delay and epilepsy were in the 12-24 month age group (Table 7-11). The greatest number of children with congenital heart disease, diarrheal disease, general surgery, pneumonia and upper airway obstruction were in the 1-12 month category.

Table 7-12 Relationship of Caregiver to Child per Condition Group

Caregiver	**AI** (n=60)	**CI** (n=60)	**TD** (n=67)	**Total** (n=187)
Mother	55	49	65	169
Father	3	5	1	9
Grandmother	2	1		3
Aunt		3		3
Foster Mother		1	1	2
Sister		1		1

Chi-sq = 15.54 (p=0.114)

The majority of caregivers across condition groups were mothers as seen in Table 7-12. The Chi-squared test indicated that the relationship of the caregiver to the child did not differ by condition groups and the relationship of the caregiver to the child was independent of condition groups (Chi-sq=15.54 and p=0.114).

Table 7-13 Event which Upset the Child per Condition Group

Event	**AI**(n=60)	**CI** (n=60)	**TD** (n=60)
Nothing of note	45	52	58
Being in Hospital	6		
Hospital Procedure	5		
Family issues		1	2
Being away from home	1	1	
Birth of sibling			2
Family member in hospital			2
Car accident	1		
Seizures	1		
Stomach Pain	1		
Abuse		1	
Burnt arm		1	
Change in Diet		1	
Tooth extraction		1	
Having an injection		1	
Separation from Mom and Dad		1	1
Sick			1
Sleep over at friend			1
Visit to the Physio			1

(n=187)

Caregivers reported the most events which they thought had upset their child in the last week in AI children (Table 7-13). These events were mostly related to the fact that they were in hospital, the procedures which they had in hospital, symptoms of their illness or missing home. Events which upset children who were CI were noted to be related to social issues (abuse, family issues) and complaints of procedures such as tooth extraction and injections. Event which upset children who were TD ranged from family members being hospitalised, family issues, ill health, or temporary separation from a parent.

Table 7-14 Event which Upset the Caregiver per Condition Group

Event	**AI**(n=60)	**CI** (n=60)	**TD** (n=60)
No event of note	42	48	60
Child in hospital	11		1
Marital/Relationship Problems	2	4	
Missing Home	3		
Work Stress		2	1
Abuse		1	
Birth of child			1
Child had a CTB last week		1	
Father admitted to hospital			1
Financial Stress		1	1
General Stress	1	1	
Hearing that one of the children at the hospital passed away		1	
Husband left to work away			1
Loss of pet			1
Surgery of child	1		
Unemployed		1	

(n=187)

The highest number of events which upset the caregivers were those who had children who were AI, most of this was attributed to the fact that their child was in hospital or they were missing home (Table 7-14). There was a high burden of marital/relationship problems for caregivers of CI children. The range of events in caregivers of TD children ranged from having a child, family being hospitalised, loss of a pet, husband working away and work stress.

Table 7-15 Diagnosis of Caregiver Across Condition Groups

	AI(n=60)	**CI** (n=60)	**TD** (n=60)	**Total** (n=187)
Nothing	46	46	50	142
HIV	7	3		10
Diabetes Mellitus	1	4	2	7
Hypothyroidism		3	3	6
Generalised Anxiety Disorder	1		3	4
Hypertension	1	3		4
Depression	1	1	1	3
Other	3	6	7	16
Total	60	66	66	192

*(n=187) *Note that some caregivers had multiple diagnoses*

Medical conditions suffered by caregivers were well distributed according to the condition group in which their child was categorised (Table 7-15). There were a high number of caregivers with hypertension, diabetes mellitus, RVD + and generalised anxiety disorder. The category of other included but was not limited to: TB, rheumatoid disease, haematological disease, lower back pain, migraines, hyperlipidaemia, endometriosis and pregnancy.

7.4.2 Feasibility and Responsiveness of the HRQoL-6D-IT

The feasibility of the HRQoL-6D-IT is determined by calculating the percentage of missing values in both the dimensions as well as the VAS. Table 7-16 below shows that there was no missing data for either the dimensions or VAS of the HRQoL-6D-IT.

All measures were completed in full by all caregivers except the FLACC pain scale (Table 7-16). The FLACC pain scale was not completed by seven caregivers of TD children.

Table 7-16 Frequency of Completion and Missing Data for Each Measure Across Condition Groups

Measure		**Frequency of completion**			**Missing Data**
		AI (n=60)	CI (n=60)	TD (n=67)	
HRQoL -6D-IT	Dimensions	60	60	67	
	VAS	60	60	67	
ASQ	Communication	60	60	67	
	Gross Motor	60	60	67	
	Fine Motor	60	60	67	
	Personal Social	60	60	67	
	Problem Solving	60	60	67	
FLACC		51	58	59	7
NIPS		9	2	1	
Diet History		60	60	67	
EQ-5D-3L	Dimensions	60	60	67	
	VAS	60	60	67	

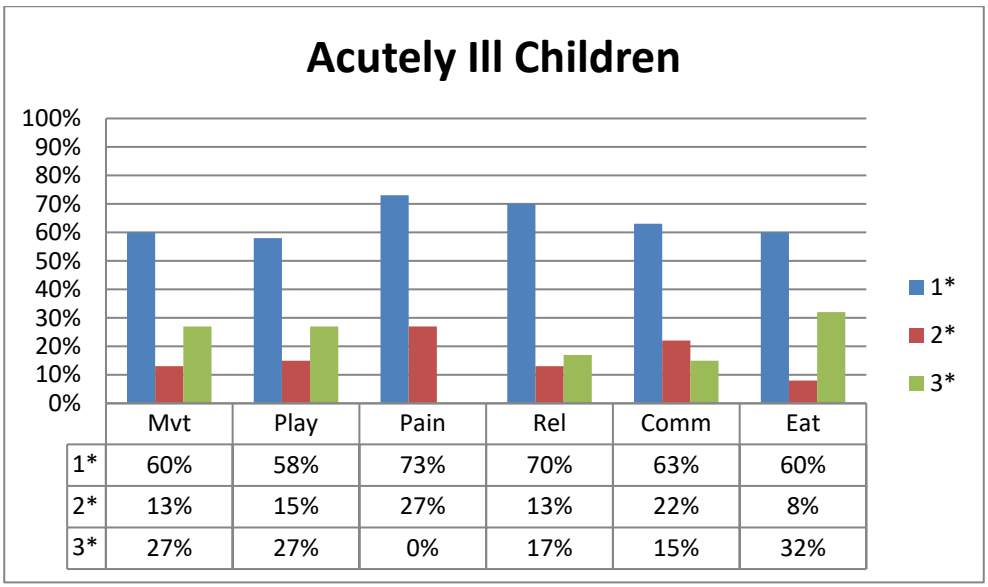
*(n=187) *FLACC was completed by caregivers of children 2-36 months, NIPS was completed by caregivers of children 1-2 months*

The frequency of responses across condition groups was analysed in Table 7-17 below. The responses to each dimension were significantly associated with condition groups for all six of the dimensions. TD children reported ≥88% of no problems and 0% for a lot of problems; for all dimensions except eating (no problems = 75%; a lot of problems= 3%).

Table 7-17 Dimension Scores of the HRQoL-6D-IT Across Condition Groups

Dimensions		**AI** (n=60)	**CI** (n=60)	**TD** (n=67)	**Total** (n=187)	**Chi-Sq**	**P-value**
Mvt	1*	36	31	64	131	35.72	***<0.001***
		60%	52%	96%	70%		
	2*	8	14	3	25		
		13%	23%	4%	13%		
	3*	16	15	0	31		
		27%	25%	0%	17%		
Play	1*	35	36	64	135	30.02	***<0.001***
		58%	60%	96%	72%		
	2*	9	11	3	23		
		15%	18%	4%	12%		
	3*	16	13	0	29		
		27%	22%	0%	16%		
Pain	1*	44	53	60	157	12.44	***0.014***
		73%	88%	90%	84%		
	2*	16	5	6	27		
		27%	9%	9%	14%		
	3*	0	2	1	3		
		0%	3%	1%	2%		
Rel	1*	42	41	59	142	13.42	***0.009***
		70%	68%	88%	76%		
	2*	8	9	8	25		
		13%	15%	12%	13%		
	3*	10	10	0	20		
		17%	17%	0%	11%		
Comm	1*	38	33	59	130	27.14	***<0.001***
		63%	55%	88%	70%		
	2*	13	9	8	30		
		22%	15%	12%	16%		
	3*	9	18	0	27		
		15%	30%	0%	14%		
Eat	1*	36	42	50	128	21.06	***<0.001***
		60%	70%	75%	68%		
	2*	5	8	15	28		
		8%	13%	22%	15%		
	3*	19	10	2	31		
		32%	17%	3%	17%		

1 No problem, 2* some problems, 3* A lot of problems Colour gradient: Red=highest number of responses*

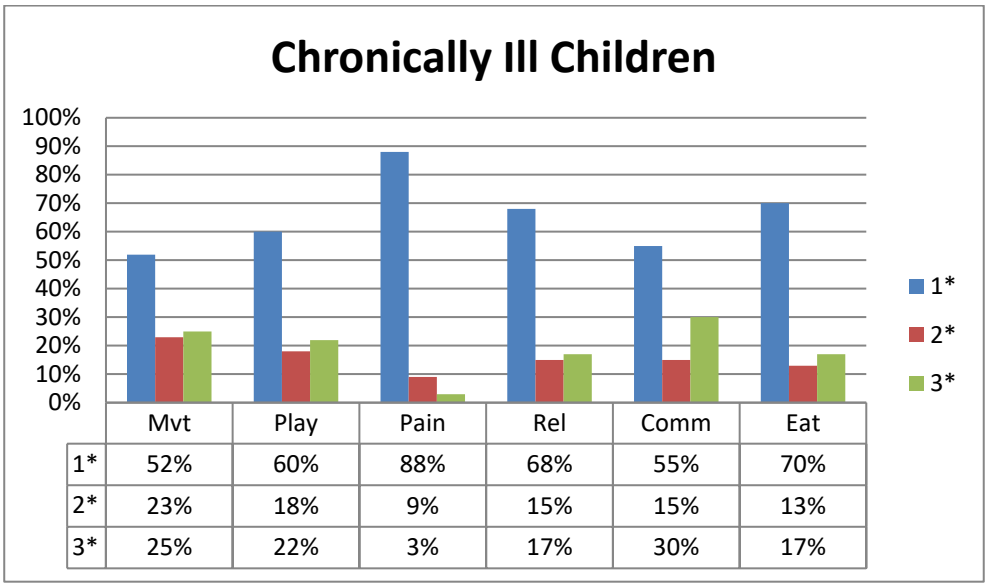


	Mvt	Play	Pain	Rel	Comm	Eat
1*	60%	58%	73%	70%	63%	60%
2*	13%	15%	27%	13%	22%	8%
3*	27%	27%	0%	17%	15%	32%

Figure 7-1 HRQoL-6D-IT Dimension Scores for AI Children

1 no problem; 2* some problems, 3* a lot of problems (n=60)*

The scores of AI children are similar across all dimensions with the reporting of no problems ranging between 58% -73% (Figure 7-1). No ceiling or floor effects were noted. Caregivers tended to report extremes (no problem or a lot of problems) for dimensions of mvt, play, relationship and eating. There was no one reported in acute care with a lot of pain.

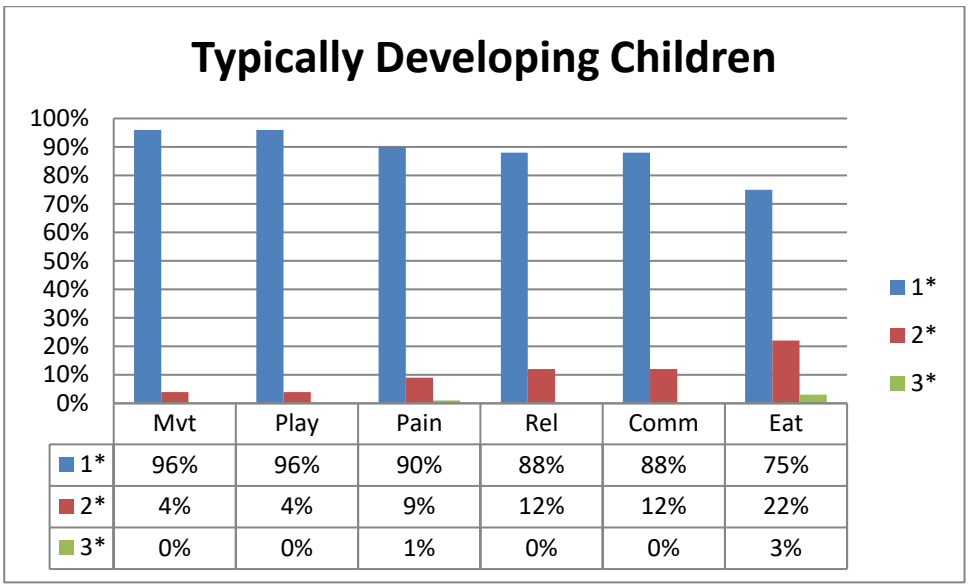


	Mvt	Play	Pain	Rel	Comm	Eat
1*	52%	60%	88%	68%	55%	70%
2*	23%	18%	9%	15%	15%	13%
3*	25%	22%	3%	17%	30%	17%

Figure 7-2 HRQoL-6D-IT Dimension Scores for CI Children

1 no problem; 2* some problems, 3* a lot of problems (n=60)*

Figure 7-2 shows that there was a ceiling effect for children experiencing no pain in CI children. Caregivers tended to report extremes (no problems or a lot of problems) for all dimensions except pain.

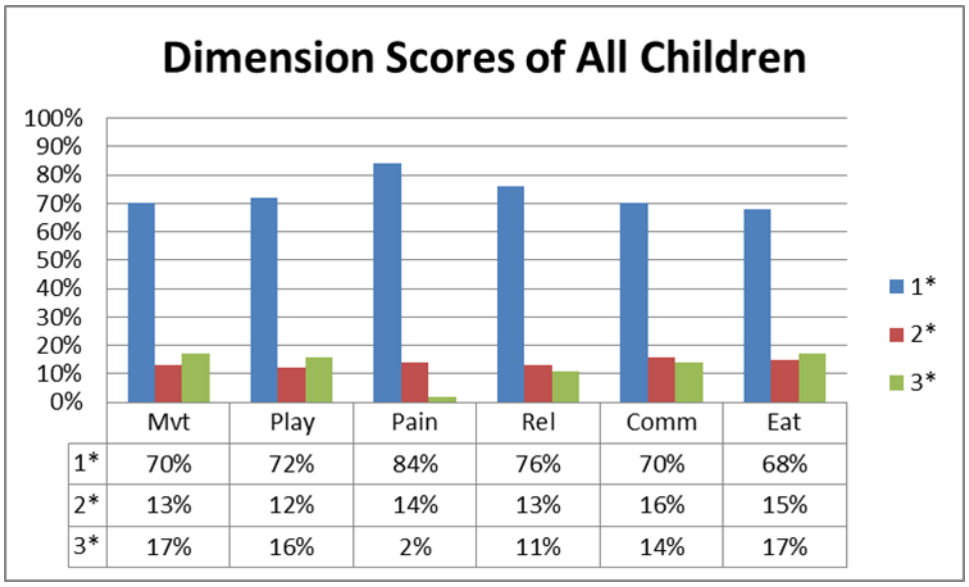


	Mvt	Play	Pain	Rel	Comm	Eat
1*	96%	96%	90%	88%	88%	75%
2*	4%	4%	9%	12%	12%	22%
3*	0%	0%	1%	0%	0%	3%

Figure 7-3 HRQoL-6D-IT Dimension Scores for TD Children

1 no problem; 2* some problems, 3* a lot of problems (n=67)*

TD children were reported as having majority of no problems across all dimensions (Figure 7-3). There were few reports of a lot of problems for pain (3%) and eating (1%). There was an incremental increase in the reporting of some problems across dimensions with physical dimensions of mvt, play, comm having the least report of problems and dimensions of pain, relationships and eating having the most report of some problems or a lot of problems.

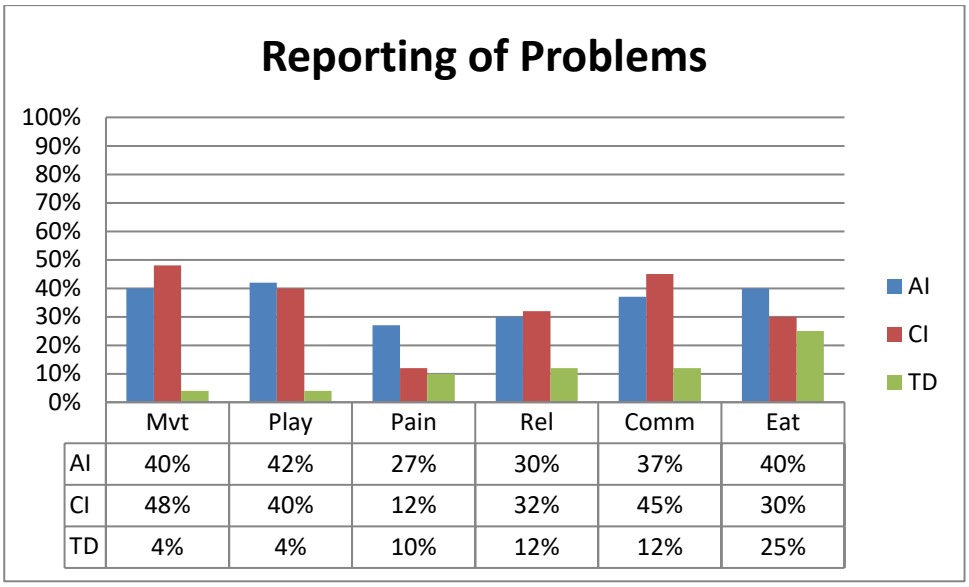


	Mvt	Play	Pain	Rel	Comm	Eat
1*	70%	72%	84%	76%	70%	68%
2*	13%	12%	14%	13%	16%	15%
3*	17%	16%	2%	11%	14%	17%

Figure 7-4 HRQoL-6D-IT Dimension Scores for All Children

1 no problem; 2* some problems, 3* a lot of problems (n=187)*

As seen in Figure 7-4 the reporing of no problems for all children in the dimensions was well distributed (68%-84%). There were no ceiling or floor effects noted. The lowest reporting for a lot of problems was for the dimension of pain (2%).



	Mvt	Play	Pain	Rel	Comm	Eat
AI	40%	42%	27%	30%	37%	40%
CI	48%	40%	12%	32%	45%	30%
TD	4%	4%	10%	12%	12%	25%

Figure 7-5 Percentage of Problems Reported on HRQoL-6D-IT Dimensions Across Condition Groups

(N=187) Chi-sq, p-values: mvt (33.7, p<0.001), play (28.35, p<0.001), pain (7.44, p=0.024), rel (8.44, p=0.015), comm (17.92, p<0.001), eating (3.23, p=0.198), (AI n=60, CI n=60, TD n=67)

The chi-square test indicated that the percentage of reporting no problem differed by condition groups for all dimensions except eating (Figure 7-5). AI children reported a higher number of problems than CI children for all dimensions except for dimensions of mvt, rel and comm.

7.4.3 Performance of the HRQoL-6D-IT Across the Age Groups

Table 7-18 Proportion of Problems Reported for HRQoL-6D-IT Dimensions for All Children per Age Group

		Mvt	Play	Pain	Rel	Comm	Eat
1-12 months (n= 58)	Problems	18	16	10	12	14	22
	No Problems	40	42	48	46	44	36
	Proportion of Problems	0.31	0.28	0.17	0.21	0.24	0.38
	CI	0.21	0.18	0.1	0.12	0.15	0.27
		0.44	0.4	0.29	0.33	0.37	0.51
12-24 months (n=55)	Problems	21	18	10	12	21	13
	No Problems	34	37	45	43	34	42
	Proportion of Problems	0.38	0.33	0.18	0.22	0.38	0.24
	CI	0.27	0.22	0.1	0.13	0.27	0.14
		0.51	0.46	0.3	0.34	0.51	0.36
24-36 months (n=74)	Problems	17	18	10	21	22	24
	No Problems	57	56	64	53	52	50
	Proportion of Problems	0.23	0.24	0.14	0.28	0.3	0.32
	CI	0.15	0.16	0.08	0.19	0.21	0.23
		0.34	0.35	0.23	0.4	0.41	0.44

Colour gradient: Red=highest number of responses

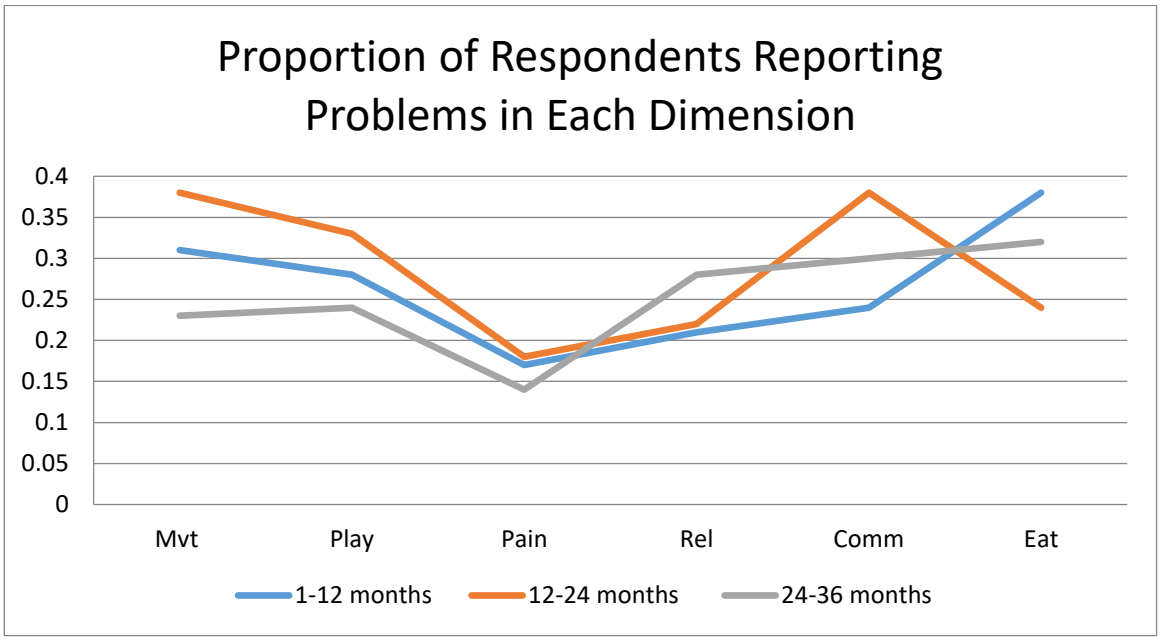


Figure 7-6 Proportion of Problems Reported for HRQoL-6D-IT Dimensions for All Children per Age Group

The proportion of problems reported for dimensions of movement, play and communication are all increased for the 12-24 month age group (Table 7-18 and Figure 7-6). There are no other obvious age

related changes in the proportion of reporting problems across age groups. The 95% confidence intervals overlap for all age-groups across all dimensions.

Movement had the highest proportion of problems reported in the 1-12 month and 24-36 month age groups for CI children (Table 7-19). Proportion of problems with play spiked in the older two age groups for AI children. The proportion of problems with relationships spiked in the youngest and oldest age group for AI children. The proportion of problems with communication spiked for CI children in the youngest and oldest age group.

Table 7-19 Proportion of Problems for Each of the HRQoL-6D-IT Dimensions Across Condition Groups and Age Group

		Mvt	**Play**	**Pain**	**Rel**	**Comm**	**Eat**
1-12 months (n=58)	AI (n=38)	0.26	0.29	0.24	0.26	0.26	0.45
	CI (n=14)	0.57	0.36	0.07	0.14	0.29	0.29
	TD (n=6)	0.00	0.00	0.00	0.00	0.00	0.17
12-24 months (n=55)	AI (n=12)	0.45	0.67	0.42	0.25	0.67	0.25
	CI (n=23)	0.43	0.39	0.17	0.35	0.52	0.26
	TD (n=20)	0.00	0.05	0.00	0.00	0.00	0.20
24-36 months (n=74)	AI (n=10)	0.30	0.60	0.20	0.50	0.40	0.40
	CI (n=23)	0.48	0.43	0.09	0.39	0.48	0.35
	TD (n=41)	0.07	0.05	0.15	0.17	0.00	0.00

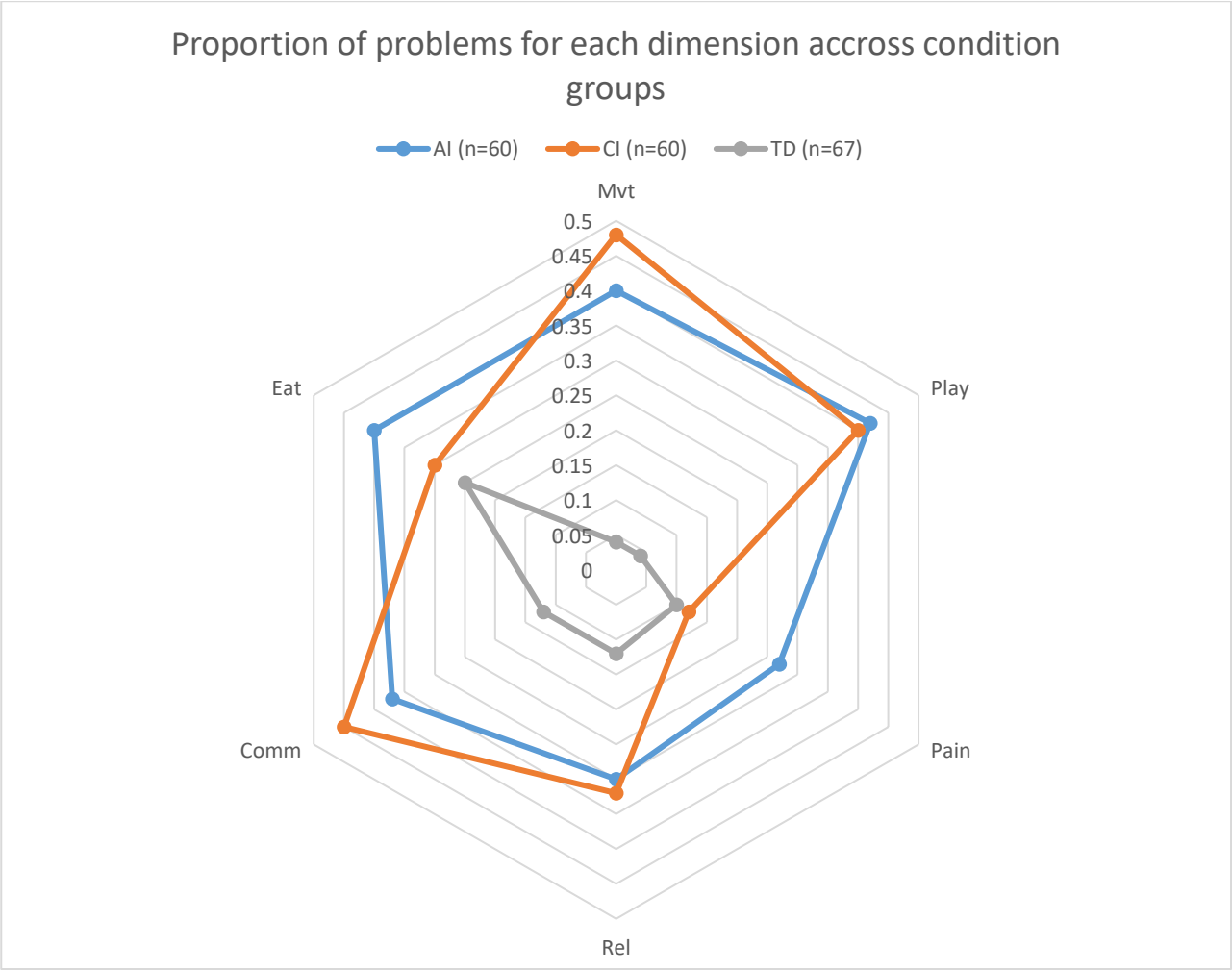


Figure 7-7 Proportion of Problems for Each of the HRQoL-6D-IT Dimensions Across Condition Groups

The proportion of problems reported is highest for AI children in dimensions of play, pain and eating (Figure 7-7). The proportion of problems reported is highest for CI children in dimensions of movement, relationships and communication.

7.4.4 Factor Structure, Reliability and Internal Consistency of the HRQoL-6D-IT

Table 7-20 Factor Analysis of the HRQoL-6D-IT (Varimax Normalised)

N=187	**Activity and Participation**	**Body Functions**
Movement	0.86	0.10
Play	0.89	0.21
Pain	0.04	0.87
Relationships	0.78	0.20
Communication	0.86	0.16
Eating	0.30	0.68
Expl.Var	2.98	1.34
Prp.Totl	0.50	0.22

	Eigenvalue	% Total variance	Cumulative Eigenvalue	Cumulative %
Factor 1	3.31	55.16	3.31	55.16
Factor 2	1.02	16.94	4.33	72.10

There were two factors which emerged and can be linked to the ICF domains of activity and participation (movement, play, relationships and communication) and body functions (pain and eating) (Table 7-20). Activity and participation accounted for 55% of the variance and body functions accounted for 17% of the variance). Body functions comprising of pain and eating are the two dimensions which are related to illness as categorized by AI and CI children.

Table 7-21 Internal Consistency and Reliability of the HRQoL-6D-IT and the Dimensions as Tested by Cronbach's Alpha

N=187	**Item-test correlation**	**Item-rest correlation**	**Average Inter –item covariance**	**Alpha if item removed**
Movement	0.82	0.71	0.20	0.79
Play	0.88	0.81	0.19	0.76
Pain	0.43	0.31	0.30	0.85
Relationships	0.79	0.68	0.22	0.79
Communication	0.84	0.74	0.20	0.78
Eating	0.61	0.42	0.25	0.85
Alpha of the Questionnaire				**0.83**

The overall reliability of the scale was good with α=0.83 [176]. Dimensions of pain and eating were shown to increase reliability if removed (Table 7-21). The item-rest correlation for pain (0.31) and eating (0.42) are

also lower. This is in keeping with the factor analysis of the HRQoL-6D-IT in that pain and eating formed a second factor on the scale (Table 7-20).

7.4.4.1 Test-Retest Reliability of the HRQoL-6D-IT

Table 7-22 Descriptive Statistics for the Participants who Participated in the Re-Testing of the HRQoL-6D-IT

Age Group (months)	1-12	1
	12-24	6
	24-36	16
Gender	Female	11
	Male	12
Caregiver	Mother	23

(n=23)

Test-retest reliability was only done in 23 TD children. As seen in Table 7-22 all of the caregivers who participated in the re-testing of the HRQoL-6D-IT were mothers. There were more children in the 24-36 age groups who participated in the re-test which is consistent with the age of the TD children who participated in the study. Results were equally spread between male and female.

Table 7-23 Frequency of HRQoL-6D-IT Dimension Scores for Test and Re-test of TD Children

			HRQoL-6D-IT dimension scores of re-test									
			Mvt	**Play**	**Pain**		**Rel**		**Comm**		**Eat**	
			1*	1*	1*	2*	1*	2*	1*	2*	1*	2*
HRQoL-6D-IT dimension scores of first test	**Mvt**	1*	23									
	Play	1*		23								
	Pain	1*			19	1						
		2*			3	0						
	Rel	1*					20					
		2*					1	2				
	Comm	1*							19			
		2*							2	2		
	Eat	1*									17	0
		2*									2	4

1 No problem, 2* some problem (n=23)*

There is very little variance in the dimension scores of the TD children participating in the test-retest of the HRQoL-6D-IT as most of the scored no problem in the dimension (Table 7-23). As the numbers were so small no statistical tests were done. However, in those with variance, the percentage agreement was calculated: pain =83%, relationships = 87%, communication=83% and eating =74%. Dimensions of

movement and play showed no variance. Variance would have been higher in AI or CI children. However, the condition of AI children changes too rapidly. CI children may have performed better with a shorter time interval between test and re-test.

7.4.5 Item Response Theory (IRT) Analysis of the HRQoL-6D-IT

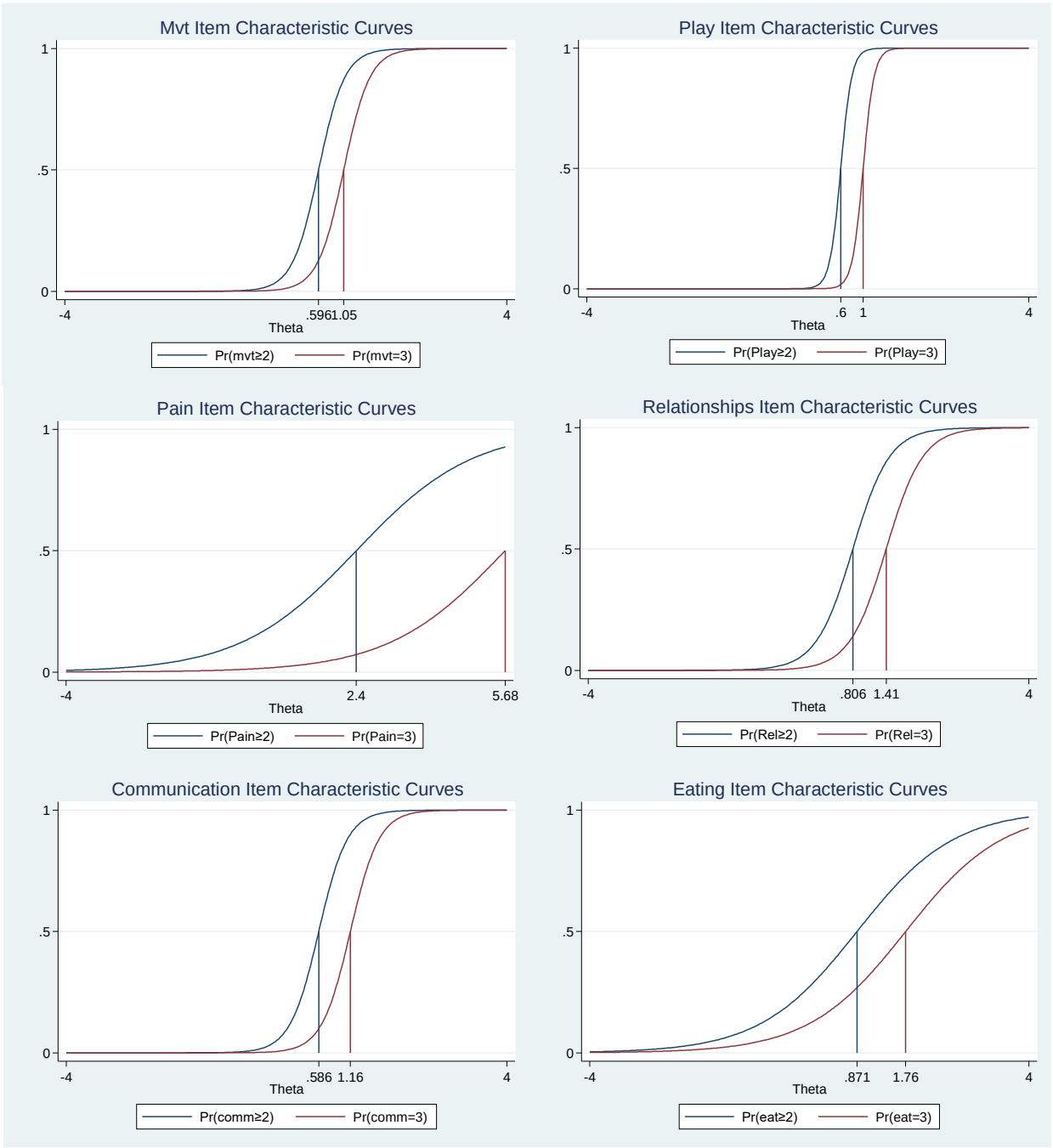


Figure 7-8 Item Characteristic Curves for the HRQoL-6D-IT Dimensions

The Item Characteristic Curves demonstrates an 'S-curve' for the probability and thus all of these dimensions demonstrate monotonicity (Figure 7-8). The difference between the theta value with a 50% probability of moving from no to some problems and that of moving from some to lots of problems ranges between 0.40 – 0.89 for all dimensions except pain (3.28). It can thus be seen that similar number of respondents reported some problem throughout the dimensions with theta ranging between 0.6 -0.87 for all dimensions except pain. With regard to discriminating between some and a lot of problems pain demonstrated the greatest change in theta required to move from the one level to the other.

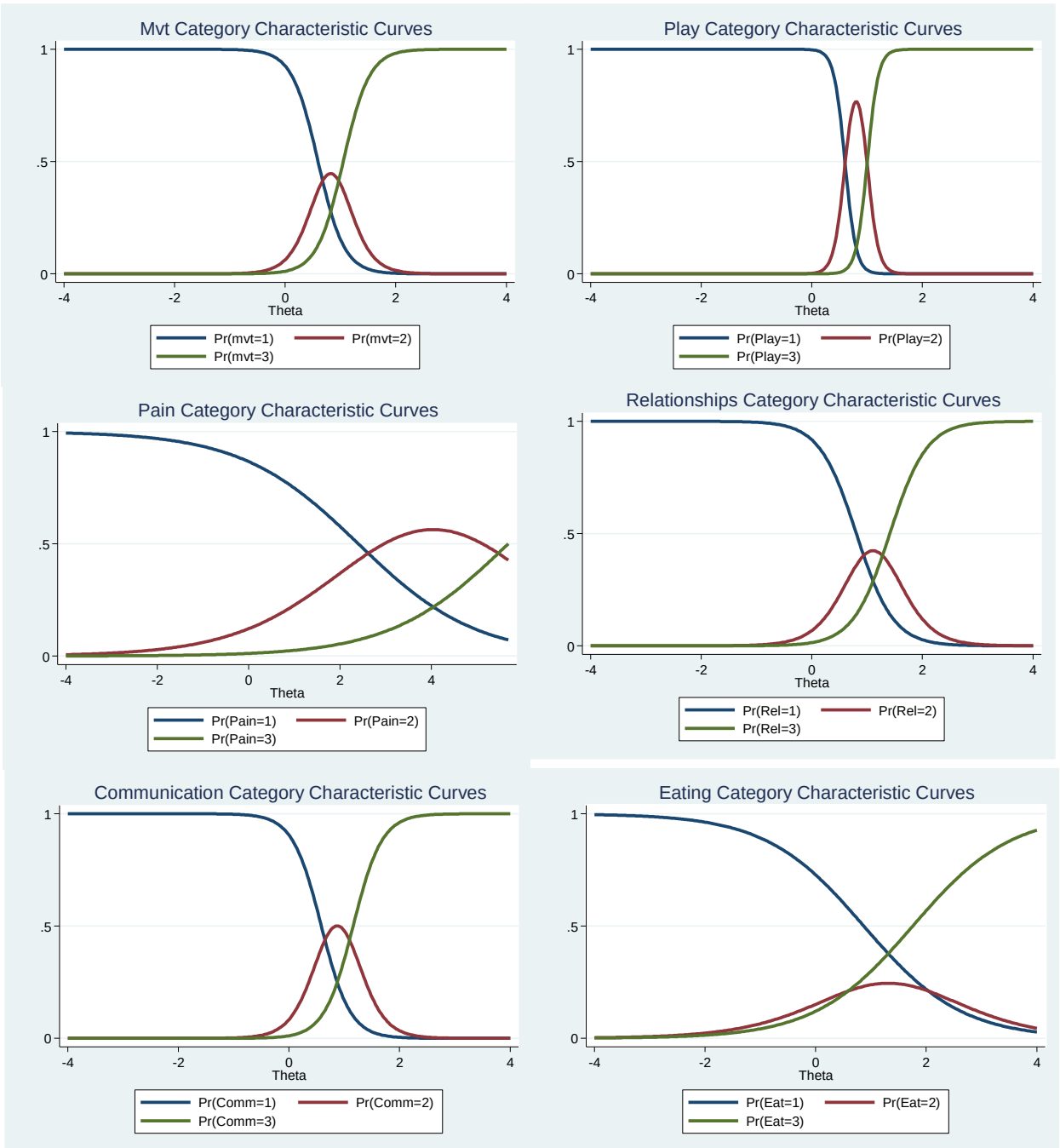


Figure 7-9 Order of the Thresholds per HRQoL-6D-IT Dimension

The thresholds are ordered for all dimensions except for eating (Figure 7-9). Some problems and a lot of problems with eating intersect first, no problems and a lot of problems with eating intersect second and no problems and some problems with eating intersect last. This could be due to the high number of TD children (25%) scoring problems with the dimension of eating (Figure 7-4). The Characteristic Curve for eating is repeated below excluding TD children (Figure 7-10). The Curve for pain is situated at a higher theta (toward the right) due to the fact that very few children were scored a lot of problems with pain.

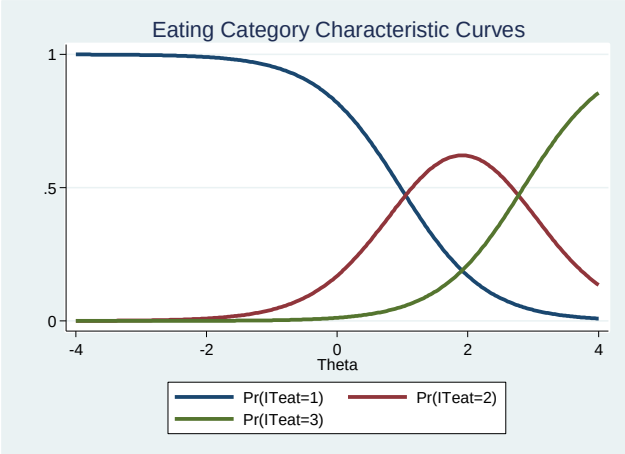


Figure 7-10 Eating Characteristic Curve for AI and CI Children

Repeating the Category Characteristic Curve for eating for AI and CI children only reveals ordered thresholds (Figure 7-10).

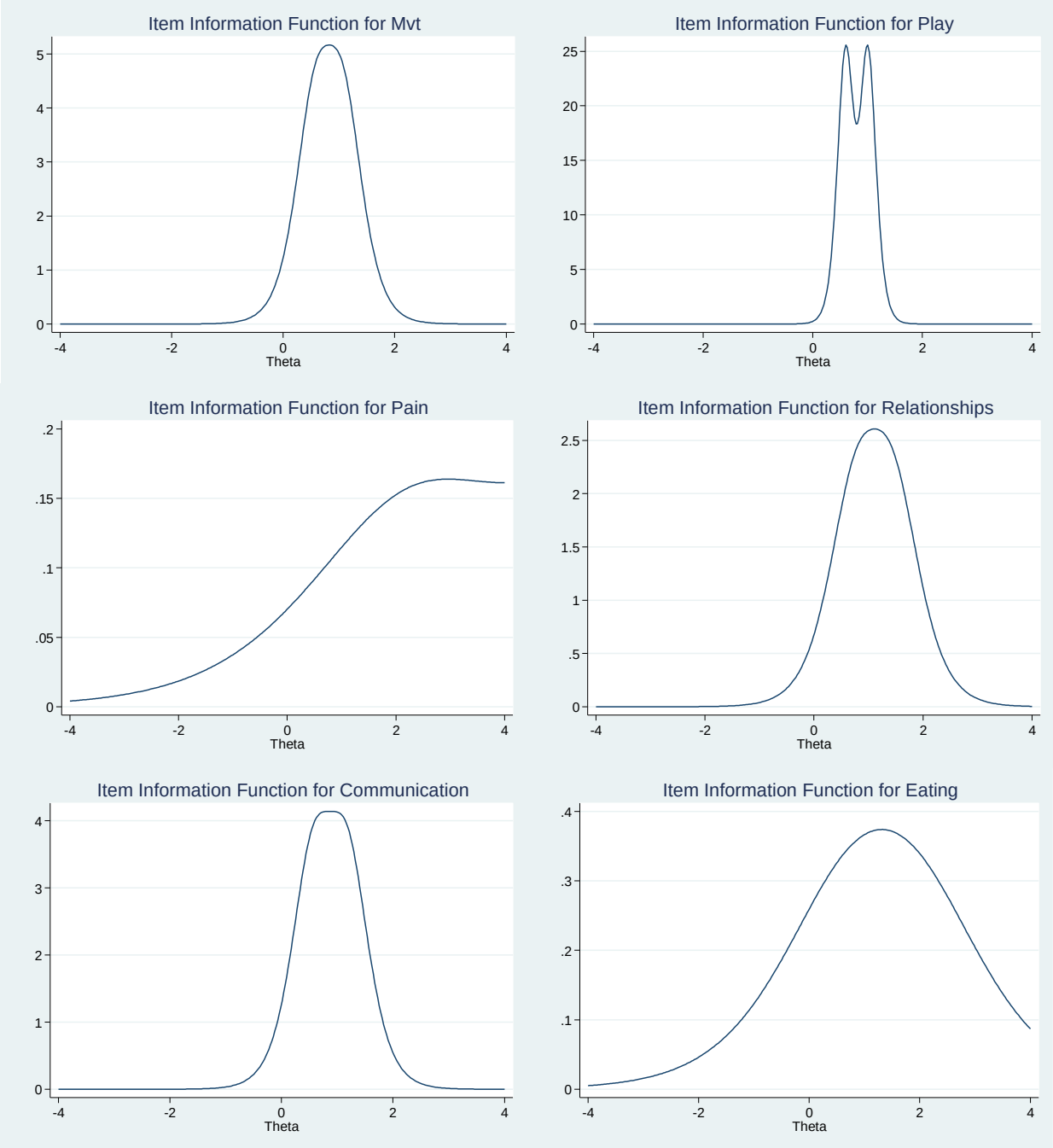


Figure 7-11 Item Information Function per HRQoL-6D-IT Dimension

The item information curves show that dimensions of mvt, play, relationships and communication add more information to the overall scale with a steep slope of the curve (slope >1) (Figure 7-11). Dimensions of eating and pain contribute different information to the overall scale (slope <0.5) which is in keeping with the two factors which emerged during factor analysis as seen in Table 7-20. The shape of the graph for play is due to the fact that most children were scored either as having no problems with or a lot of problems with play. The shape of the graph for eating is due to the fact that very few children were scored a lot of problems with pain.

7.4.6 Statistics to Determine Validity

7.4.6.1 Dimensions of the HRQoL-6D-IT

Table 7-24 Correlation of HRQoL-6D-IT Movement Dimension and ASQ Gross Motor Domain

N=187		ASQ Gross Motor			Total
		1*	2*	3*	
HRQoL-6D-IT Mvt	1*	119	7	5	131
	2*	8	8	9	25
	3*	1	4	26	31
Total		128	19	40	187

1 No problem, 2* Some problems, 3* A lot of Problems. Kappa = 0.61 (p<0.001)*

The dimension scores of movement on the HRQoL-6D-IT was significantly correlated with the dimension scores of the ASQ gross motor domain (kappa=0.61 and p<0.001) (Table 7-24). There were slightly more caregivers reporting that their child had a lot of problems on the Gross Motor Domain of the ASQ. This could be attributed to the fact that the ASQ questions are far more specific than the HRQoL-6D-IT and caregivers may not recognise all of those attributes as being 'age appropriate' attributes.

Table 7-25 Correlation of HRQoL-6D-IT Play Dimension and ASQ Fine Motor and Problems Solving Domains

N=187		ASQ Fine Motor & Problem Solving			Total
		1*	2*	3*	
HRQoL-6D-IT Play	1*	123	4	8	135
	2*	7	9	7	23
	3*	3	4	22	29
Total		133	17	37	187

1 No problem, 2* Some problems, 3* A lot of Problems. Kappa = 0.60 (p<0.001)*

The dimension scores of play on the HRQoL-6D-IT was significantly correlated with the dimensions scores of the ASQ fine motor and problem solving domains (kappa=0.60 and p<0.001) (Table 7-25). Similarly to the dimension of movement there is a slight discrepancy between the rating of some and a lot of problems measured by the ASQ and HRQoL-6D-IT.

Table 7-26 Correlation of HRQoL-6D-IT Pain Dimension and FLACC and NIPS

N=187		FLACC and NIPS score			Total
		1*	2*	3*	
HRQoL-6D-IT Pain	1*	108	41	1	150
	2*	4	20	3	27
	3*	1	1	1	3
Total		113	62	5	180

1 No problem, 2* Some problems, 3* A lot of Problems. Kappa = 0.33 (p<0.001)*

The dimension scores of pain on the HRQoL-6D-IT was significantly correlated with the FLACC pain scale score (children 2 -36 months) and the NIPS pain scale score (children 1-2 months) (kappa=0.33 and p<0.001) (Table 7-26). There was a higher reporting of pain on the NIPS and FLACC pain scale than on the HRQoL-6D-IT. This could be attributed to the fact that behavioural characteristics were interpreted outside of the context of pain on the NIPS and FLACC pain scale. One of the criteria for consolability on the FLACC pain scale read "Reassured by occasional touching, hugging or talking to. Distractible" which could have been attributed to general behaviour after something had upset the child rather than behaviour in response to pain.

Table 7-27 Correlation of HRQoL-6D-IT Relationships Dimension and ASQ Personal Social Domain

N=187		ASQ Personal Social			Total
		1*	2*	3*	
HRQoL-6D-IT Rel	1*	117	17	8	142
	2*	12	9	4	25
	3*	1	4	15	20
Total		130	30	27	187

1 No problem, 2* Some problems, 3* A lot of Problems. Kappa=0.44 (p<0.001)*

The dimension scores of relationships on the HRQoL-6D-IT was significantly correlated with the scores of the ASQ personal social domain (kappa =0.44 and p<0.001) (Table 7-27). There were slight discrepancies between reporting on the HRQoL-6D-IT and the ASQ which could be attributed to the additional personal items measured in the ASQ personal social domain.

Table 7-28 Correlation of HRQoL-6D-IT Communication Dimension and ASQ Communication Domain

N=187		ASQ Communication			Total
		1*	2*	3*	
HRQoL-6D-IT Comm	1*	115	15	0	130
	2*	10	7	13	30
	3*	3	4	20	27
Total		128	26	33	187

1 No problem, 2* Some problems, 3* A lot of Problems. Kappa=0.50 (p<0.001)*

The dimension scores of communication on the HRQoL-6D-IT was significantly correlated with the scores of the ASQ communication domain (kappa =0.50 and p<0.001) (Table 7-28). The distribution of scores across severity levels on the HRQoL-6D-IT and ASQ were very similar.

Table 7-29 Correlation of HRQoL-6D-IT Eating Dimension and Diet History

N=187		**Dietary Information**			Total
		1*	2*	3*	
HRQoL-6D-IT Eating	1*	114	13	1	128
	2*	13	11	4	28
	3*	0	5	26	31
Total		127	29	31	187

1 No problem, 2* Some problems, 3* A lot of Problems. Kappa=0.60 (p<0.001)*

The dimension scores of eating on the HRQoL-6D-IT was significantly correlated with the dietary information score (Kappa =0.60 and p<0.001) (Table 7-29). The distribution of scores across severity levels on the HRQoL-6D-IT and ASQ were very similar.

7.4.6.2 VAS of the HRQoL-6D-IT

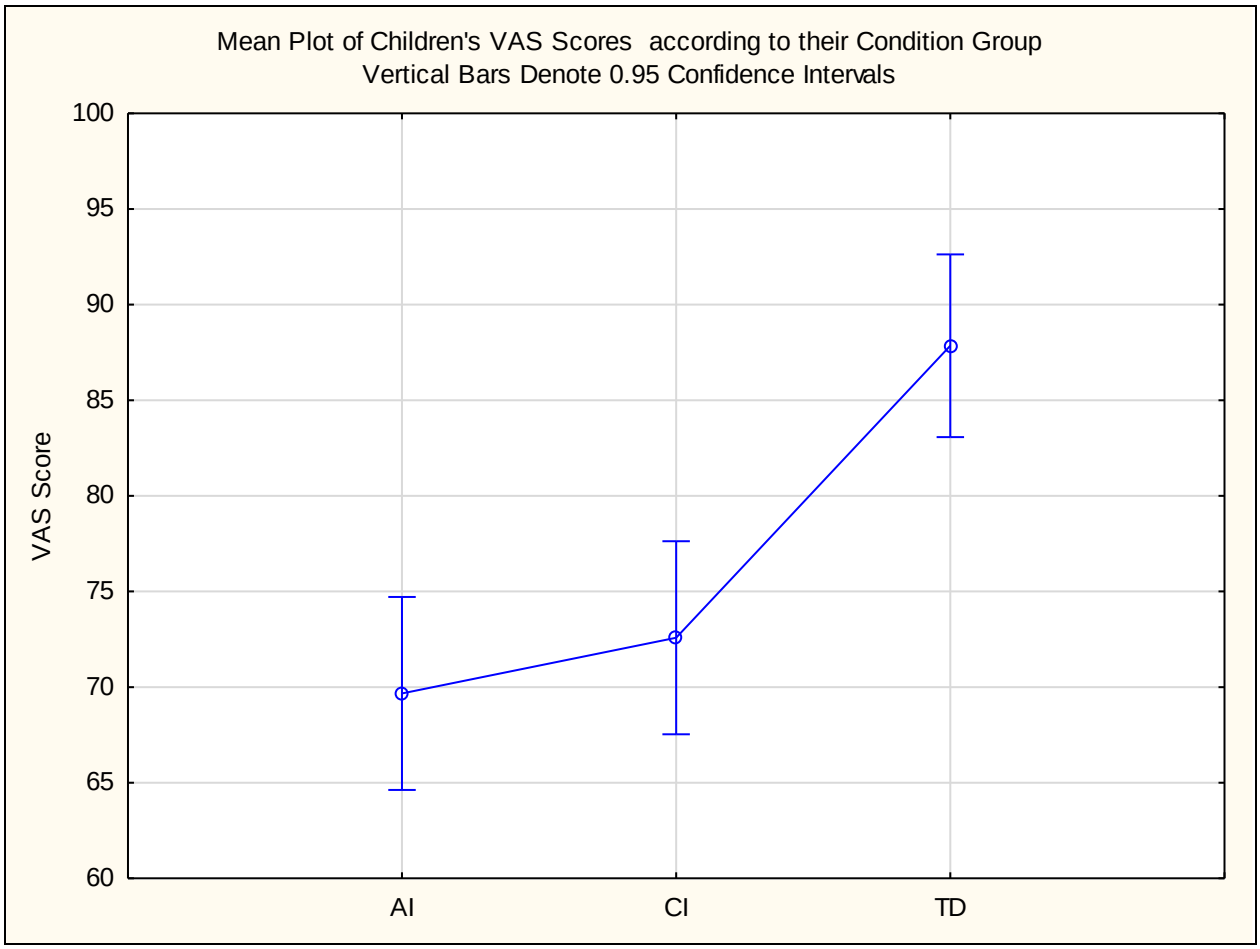


Figure 7-12 Mean Plot of Children's VAS Scores according to their Condition Group

F (2.18) = 15.65; p <0.001(N=187)

As seen in Figure 7-12 the VAS Median for AI children was 60 (IQR 0-100), CI children was 77 (IQR 15-100) and TD children was 90 (IQR 52-100). Post Hoc Tukey Analysis revealed that TD was significantly different to AI and CI ($p<0.01$) but AI and CI were not different (Table 7-30).

Table 7-30 Post Hoc Tukey Analysis of HRQoL-6D-IT VAS scores

	AI Mean VAS score 69.67	CI Mean VAS score 72.58	TD Mean VAS score 87.85
AI (n=60)		0.70	*<0.001*
CI (n=60)	0.70		*<0.001*
TD (n=67)	*<0.001*	*<0.001*	

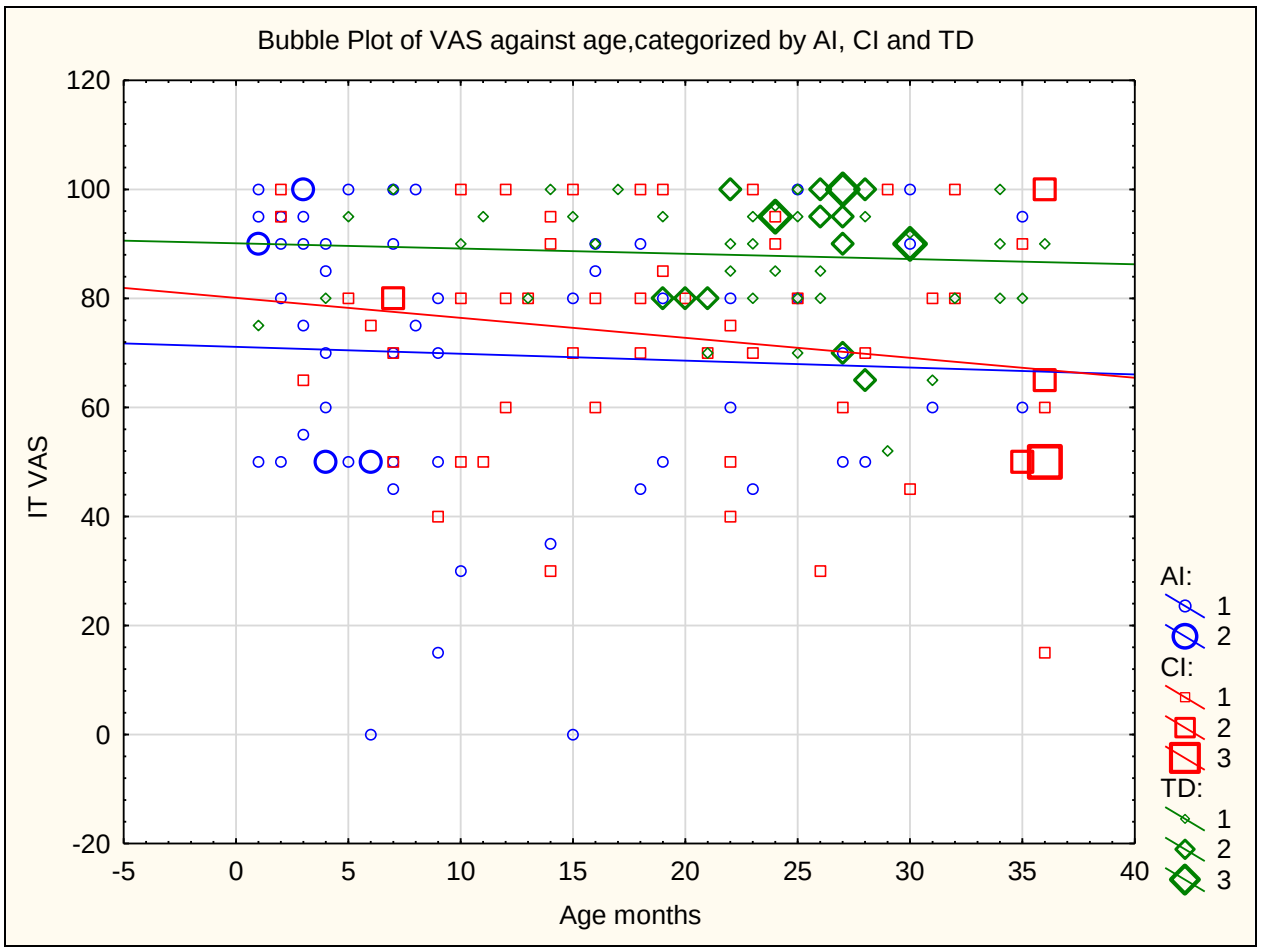


Figure 7-13 Correlation Between Age and HRQoL-6D-IT VAS Across Condition Groups

There is no significant correlation between VAS and age for any group for VAS scores AI (r= -0.05, p=0.70), CI (r=-0.18, p=0.16) or TD (r=-0.06, p=0.61) children across their age (Figure 7-13). Thus the null hypothesis can be accepted where the age of the child is not correlated to their general health score as determined by the VAS. The slope of the graph for CI children is negative indicating that their HRQoL gets worse as they get older.

Multiple regression analysis with the VAS as dependent variable and dummy variables representing the different levels of the dimensions accounted for 35% of the variance. The model improved and accounted for 45% of the variance, once nine outliers had been removed (Table 7-31).

Table 7-31 Regression Analysis of the HRQoL-6D-IT VAS Score and Dimension Scores

	b*	Std. Err. Of b*	b	Std. Err. Of b	t(164)	p-value
Intercept			88.74	1.46	60.69	0.000
Life Event of the child	-0.06	0.06	-3.26	2.97	-1.10	0.275
Mvt 2*	-0.17	0.07	-9.36	3.73	-2.51	***0.013***
Mvt 3*	-0.18	0.09	-10.30	5.22	-1.97	0.050
Play 2*	-0.03	0.07	-1.64	4.02	-0.41	0.685
Play 3*	-0.07	0.11	-4.26	5.99	-0.71	0.477
Pain 2*	-0.13	0.06	-6.92	3.39	-2.04	***0.043***
Pain 3*	-0.07	0.06	-10.90	8.75	-1.25	0.215
Rel 2*	-0.03	0.07	-1.92	3.79	-0.51	0.614
Rel 3*	-0.16	0.08	-11.64	5.74	-2.03	***0.044***
Comm 2*	-0.04	0.07	-2.21	3.67	-0.60	0.548
Comm 3*	-0.07	0.09	-4.42	5.11	-0.87	0.388
Eat 2*	-0.12	0.06	-6.38	3.12	-2.05	***0.042***
Eat 3*	-0.29	0.07	-15.11	3.51	-4.30	***<0.001***

1 No problem, 2* Some problems, 3* A lot of Problems Adjusted R^2=0.45(n=178)*

Coefficients of Mvt 2*(p=0.013), Pain 2* (p=0.043), Rel 3* (p=0.044), Eat 2* (p=0.042) and Eat 3*(p<0.001) all significantly detracted from the VAS score. All the other dimensions detracted from the VAS score. A lot of problems detracted more from the VAS score than some problems for all dimensions.

7.4.7 Influence of Factors Relating to the Caregiver on the Proxy Reporting of HRQoL of Their Child

Multiple regression analysis with the child's HRQoL-6D-IT VAS as dependent variable and dummy variables representing the different levels of the dimensions of the HRQoL-6D-IT and the caregiver's EQ-5D-3L VAS score accounted for 43% of the variance. The model improved and accounted for 53% of the variance, once ten outliers had been removed (Table 7-32). If this is compared to the model in Table 7-31 above, the addition of the caregiver's VAS accounts for 8% of the variance.

Table 7-32 Regression Analysis of Child's HRQoL-6D-IT VAS Score and Dimension Scores and the Caregivers' EQ-5D-3L VAS Scores

	b*	Std. Err. of b*	b	Std. Err. of b	t(166)	p-value
Intercept			58.06	5.9395	9.77	<0.001
Mvt 2*	-0.14	0.06	-7.99	3.1328	-2.55	***0.012***
Mvt 3*	-0.14	0.08	-7.69	4.5948	-1.67	0.096
Play 3*	-0.20	0.08	-11.34	4.7226	-2.40	***0.017***
Pain 2*	-0.10	0.06	-5.17	3.0874	-1.68	0.096
Pain 3*	-0.10	0.05	-14.45	7.8569	-1.84	0.068
Rel 2*	-0.06	0.06	-3.09	3.0282	-1.02	0.309
Rel 3*	-0.09	0.07	-6.17	4.5239	-1.36	0.174
Eat 2*	-0.15	0.05	-7.91	2.7899	-2.84	***0.005***
Eat 3*	-0.32	0.06	-16.61	3.1621	-5.25	***<0.001***
EQ VAS	0.28	0.05	0.35	0.0660	5.27	***<0.001***

1 No problem, 2* Some problems, 3* A lot of Problems Adj R^2=0.53 (n=177)*

Coefficients of the HRQoL-6D-IT dimension levels of mvt 2* (p=0.012), play 3* (p=0.017), eat 2* (p=0.005) and eat 3* (p<0.001) caregivers EQ-5D-3L VAS score (p<0.001) significantly detracted from the child's VAS.

If we consider the summary of the regression results in Table 7-33 below and examine the percentage of variance each dimension contributes, to the R-square change, one can conclude that the caregiver's general rating of health on the EQ-5D-3L VAS accounts for 10% of the variance. This is more than the variance contributed by some problems with eating (3%) and some problems with mvt (1%), but less than a lot of problems with play (25%) and eating (13%). These results will need further examination in future studies. These results further emphasises the question of whether caregivers can accurately report on their child's health. Furthermore, due to the close relationship between caregiver and child one would need to consider whether the HRQoL of both members of the dyad should be measured in the future.

Table 7-33 Summary Regression Results Showing Percentage of Variance of Each Coefficient

	Step +in/-out	Multiple R	Multiple R-square	R-square change	F - to entr/rem	p-value	Variables included
Play 3*	1	0.50	0.25	**0.25**	59.37	0.000	1
Eat 3*	2	0.62	0.39	**0.13**	37.35	0.000	2
EQ-5D-3L VAS	3	0.69	0.48	**0.10**	31.85	0.000	3
Eat 2*	4	0.72	0.52	**0.03**	12.12	0.001	4
Mvt 2*	5	0.73	0.53	**0.01**	4.30	0.040	5
Pain 3*	6	0.73	0.54	0.01	3.64	0.058	6
Mvt 3*	7	0.74	0.55	0.01	3.64	0.058	7
Pain 2*	8	0.74	0.55	0.01	3.15	0.078	8
Rel 3*	9	0.75	0.56	0.00	1.45	0.231	9
Rel 2*	10	0.75	0.56	0.00	1.04	0.309	10

1 No problem, 2* Some problems, 3* A lot of Problems (n=177)*

7.5 Discussion and Conclusions

The aim of this study was to examine the reliability and validity of the newly developed measure, the HRQoL-6D- IT. The HRQoL-6D- IT was targeted at children from 1-36 months of age; it had six dimensions and used the behaviour of 'at an age appropriate level' as a universal descriptor, apart from pain which was referenced to the child's usual behaviour. The objectives were met. Table 7-34 summarises the performance of each of the dimensions. The dimensions all had moderate to high discriminability thresholds were all ordered, except for eating which was only ordered in analysis of the AI and CI children. The two factor model was confirmed in that mvt, play, relationships and communication added more information to the scale than did pain and eating. The dimensions appeared to perform well across the age groups, with little sign of a trend in the proportion reporting problems from youngest to oldest. The six dimensions and VAS could discriminate between known groups, demonstrated concurrent validity against established measures and was internally consistent and thus reliable. The test-retest reliability was not adequately established as there was so little variance in the reports of the respondents. Each level of problem of each dimension detracted from the VAS in multiple regression analysis, with a lot of problems detracting more than some problems. It is thus concluded that the HRQoL-6D- IT is a valid and reliable measure for monitoring HRQoL in children from 1-36 months of age.

Table 7-34 Summary of the Performance of the HRQoL-6D-IT Dimensions

		Mvt	Play	Pain	Rel	Comm	Eat
	Feasibility	No missing data	No missing data	No missing data	No missing data	No missing data	No missing data
	Responsiveness in AI children	No floor/ ceiling effects	No floor/ ceiling effects	No floor/ ceiling effects	No floor/ ceiling effects	No floor/ ceiling effects	No floor/ ceiling effects
	Performance across ages	Increased proportion of problems for 12-24 months	Increased proportion of problems for 12-24 months	No difference in proportion of problems across ages	No difference in proportion of problems across ages	Increased proportion of problems for 12-24 months	No difference in proportion of problems across ages
Reliability	**Internal Consistency (item-rest)**	0.71	0.81	**Lower 0.31**	0.68	0.74	**Lower 0.42**
	Alpha if removed	0.79	0.76	0.85	0.79	0.78	0.85
	Test-retest % agreement	No Variance	No Variance	83%	87%	83%	74%
IRT	**Monotonicity**	✓	✓	✓	✓	✓	✓
	Discrimination between levels	High 0.45	High 0.4	**Poor 3.28**	High 0.33	High 0.57	High 0.89
	Order of thresholds	✓	✓	✓	✓	✓	Only for AI and CI children
Validity	**Concurrent Validity**	kappa=0.61 p<0.001	kappa=0.60 p<0.001	kappa=0.33 p<0.001	kappa=0.44 p<0.001	kappa=0.50 p<0.001	kappa=0.60 p<0.001
	Discriminant Validity	AI & CI reported the most lot of problems; TD reported the most no problems	AI & CI reported the most lot of problems; TD reported the most no problems	AI & CI reported the most lot of problems; TD reported the most no problems	AI & CI reported the most lot of problems; TD reported the most no problems	AI & CI reported the most lot of problems; TD reported the most no problems	Report of no problems similar for CI & TD. Report of some problems highest in TD. Report of lots of problems most in AI and least in TD

7.5.1 Sample

Participants were more or less equally distributed across the condition groups in terms of gender and distribution. The 1-12 month age group of children was highest for the AI children which is in keeping with the record of admissions at the children's hospital where a third of the 60 000 patient visits each year are by children younger than one year of age [327]. These children were mostly frequently hospitalised due to congenital heart disease, diarrheal disease, general surgery and pneumonia. This is similar to the global burden of disease in children where diarrheal disease and pneumonia are highlighted [36], [37]. Furthermore Africa has been reported as having the highest prevalence of childhood heart disease which includes congenital heart disease [328].

The 24-36 month age group was the largest in TD children, possibly due to the average pre-school child beginning school in the year of their third birthday [113]. The conditions reported by TD children included common diagnoses of asthma, allergy, diarrhoea and pneumonia. It is noteworthy that of the TD children one was diagnosed with cerebral palsy (hemiplegia) and one was diagnosed with foetal alcohol syndrome; both children were considered high functioning and did not require specialised schooling. The number of children with chronic illness was similar in the 12-24 and 24-36 month age groups. This could be attributed to the type of illness the children reported with the majority of children having a diagnosis of developmental delay and cerebral palsy. Although there has been an improvement in early detection of developmental delay and cerebral palsy with screening tools the majority of children were only noted as having regression in milestones when their gross motor milestones such as crawling and walking were delayed, leading to a diagnosis in their second year of life [329].

According to Statistics South Africa 42.5% of children under five years of age live with their biological mothers only [330], thus it was not surprising that the majority of caregivers in the study where mothers.

7.5.2 Feasibility and Responsiveness

The HRQoL-6D-IT did not have any missing data on the reporting of dimensions or VAS. The other measures, except for the FLACC pain scale, did not report any missing data either. The FLACC pain scale only had missing data in the TD group. This could be attributed to the fact that the researcher was available for assistance when the caregivers of AI and CI children completed the questionnaires. The reliability of the pain scores reported by caregivers and children have been explored in older children [331]. This has proven a challenge as the type of pain (acute pain, chronic, post-operative pain) and the measure could all affect the rating of pain [331]. It was however, shown that caregivers tend to underestimate pain the child experiences [331]. Measures such as the FLACC, primarily used by health care professionals [233], [296]–[298], may be more difficult for caregivers to understand and thus score. Furthermore, there is no literature available on the validation of paediatric pain scales in 'typically developing or healthy' children. The dimension of pain was however retained as it performed well across known-groups with ill children reporting more problems with a lot of pain and presence of pain significantly reduced the VAS score.

It is speculated that the caregivers rated their TD children on their general behaviour throughout the day as opposed to pain behaviour with many caregivers indicating that their child had an occasional grimace, frown, withdrawn; that they were squirming, shifting back and forth, tense regarding their activity; they had moans or whimpers, occasional complaint and that they were reassured by occasional touching, hugging or talking to.

The HRQoL-6D-IT dimensions showed good responsiveness with no ceiling or floor effects for AI children. The dimension selection and descriptions were thus appropriately constructed. These results are in contrast to the EQ-5D-Y, on which the instrument was modelled, with high report of ceiling effects [144], [145], [220], [332]–[335].

7.5.3 Performance of the HRQoL-6D-IT Across the Age Groups and Condition Groups

There was evidence of known group validity for dimension and VAS scores for AI, CI and TD children. Children who were ill (AI/CI) showed a significantly different VAS score from children who were typically developing as was expected. However, there was no difference between children with acute or chronic conditions. This could be due to the fact that the difference in acute and chronic illness is dependent on duration of illness and does not necessarily account for severity of illness. Both dimensions scores and the VAS may have shown different results if longitudinal measurement was taken to show change of health over time. Recording the severity of illness would have further assisted in establishing sensitivity of the measure.

The dimension of eating had a different pattern of response for TD children than the other dimensions. The report of no problems with eating was similar to that of CI children and the report of some problems with eating was the highest in TD children. This resulted in disordered thresholds for the dimension of eating when TD children were included in the analysis. The performance of the dimension of eating could be attributed to the prevalence of picky eating which is cited in Boquin et al (2014), as being between 8%-36% in children 24-60 months and as high as 50% in children 19-24 months [336]. Furthermore the parents perception of whether their child was a picky eater or not changed several times over a two week period [336]. However, a lot of problems with eating was associated with illness with AI children and CI children reported as having the highest problems respectively.

For caregivers to perceive the presence and intensity of pain in children is challenging as pain is interlinked with physical, emotional, behavioural and developmental factors [337]. This challenge is compounded by the fact that children below two years of age are non-verbal and children between two and three years of age can report pain but are unable to describe the intensity of the pain [338]. This may have led to the results that the percentage of children experiencing some pain was the same in CI and TD children. Caregivers did seem to rate a lot of pain less frequently and when rated it was associated with illness with CI and AI children reported as having the most problem respectively. This was supported by the relatively large difference in the theta of an individual (HRQoL) reporting some pain and a lot of pain. Eating and pain emerged as a factor of body, structure and function and a lot of problems in the dimensions relate more to

the presence of a health condition or illness. The item characteristic curves supported the emergence of this factor as eating and pain was found to contribute different information to the instrument than the other dimensions. Furthermore, the internal consistency for the dimensions of pain and eating were lower but they still contributed to the overall reliability of the scale.

From the results the HRQoL-6D-IT can be considered a 'one-size-fits-all' instrument as the dimensions and VAS performed well across all ages. The proportion of reporting problems across dimensions did show a spike in the 12-24 month old children for dimensions of movement, play and communication. This spike may be a reflection of the severity of the health condition of the sample, rather than a symptom of differential age responses as conditions of cerebral palsy, developmental delay and epilepsy were most frequently reported in this age group.

The concurrent validity results of the dimensions on the HRQoL-6D-IT were similar to results from validity testing of another HRQoL measure for pre-school children, the HSCS-PS when compared to results obtained from the Bayley Scales of Infant Development, Vinelands Adaptive Behaviour Scale and the Stanford-Binet [174]. The concurrent validity was higher for motor-related areas of function which included dimensions of movement, play, communication and eating on the HRQoL-6D-IT and items of mobility, self-care and dexterity on the HSCS-PS [174]. Furthermore, concurrent validity was lower for less tangible functions which included pain and relationships on the HRQoL-6D-IT and vision and pain/discomfort on the HSCS-PS [174]. The authors of the HSCS-PS attributed this to the caregivers' commendable capability of being able to discriminate between different aspects of function as opposed to rating all aspects of function similarly [174].

The interplay between the perceived global health rating of the caregiver and child was noteworthy as the caregiver's VAS accounted for 10% of the variance of the VAS score of the child. Thus the perceived health states of the caregiver and the child are interrelated. Theories of motor development highlight the importance of measuring the caregivers HRQoL due to the intimate interplay between caregiver and child in the development of emotion and self-regulation [108]. The effect of the caregivers health on the child's rating of health has been postulated in the literature and the effect on elicitation of preference weights has been debated [272], [339], [340]. This is noted if CUA is calculated from a societal perspective where the cost of the health intervention is calculated on the effects experienced by the patient and all other individuals that the intervention affects (such as family members) [341], [342]. This spillover effect of health between caregiver and child has been found in caregivers of children with asthma [343], [344], genetic conditions [345], Autism Spectrum Disorders [346], Spina Bifida[347] and mental health concerns [348]. The results may have been limited by the fact that the perceived rating of the child's VAS by the

caregiver could have been impacted by the caregivers own HRQoL. The proxy rating could further have been clouded by the caregiver's expectations of the child, their definition of HRQoL and their understanding of the child's illness and its sequelae [349]. The reason for problems experienced per domain in the caregiver was not sought; these reasons could have helped understand whether problems were associated with their child. It is thus recommended that future studies investigate the difference in effect if the caregiver proxy or an unrelated adult proxy rates their child's HRQoL. In addition, exploring the reasons behind the caregivers reporting problems on dimensions of the EQ-5D-3L might clarify whether the problems reported is in fact due to the child's health.

7.5.4 Study Limitations

The inclusion of TD children for reliability analysis on the test-retest of the instrument limited the analysis of the data and the subsequent results obtained. It is recommended that future studies wanting to evaluate the test-retest reliability include CI children with a shorter period between reports. This will increase the variance in the results obtained making analysis easier. Cognitive debriefing after completion of a number of the HRQoL-6D-IT measures would have been useful to further establish the comprehensibility and acceptability of the measure.

The limitations of the study include that the LSM could not be computed to determine whether SES affected the results. No other SES measure was included in the study. A further limitation was that no information regarding the caregivers' education level was collected and this could potentially have affected the results.

The study results are limited to English speaking caregivers of children who were AI, CI or TD and the results are thus not generalizable. It is recommended that future studies include caregivers from different cultural groups. The inclusion of AI and CI children could have been a limitation in selection of known groups as it accounts for duration of illness but not necessarily severity of illness. It is recommended that future studies determine known-group validity by disease severity.

7.6 Conclusion

The HRQoL-6D-IT was found to be valid and reliable for use with children aged 1-36 months in South Africa. It is recommended that future testing be done to assess the feasibility and clinical utility of the measure and to include international input in further development. Furthermore contextual data (e.g. demographic

and socio-economic information and caregiver HRQoL) should be included with future research of the measure to clarify the relationships and enhance the use of the instrument.

8 Chapter 8: Conclusion and Recommendations

Review of the literature suggested that development of a new HRQoL measure needed to include a number of sources, including qualitative research with the target population, as well as a step wise approach to developing and reducing an item bank, construction of the measure and validity and reliability testing [79], [121], [123]. The procedure followed in this study is summarised in Figure 8-1 below and is based on these recommendations and the working framework developed in Chapter 2. .

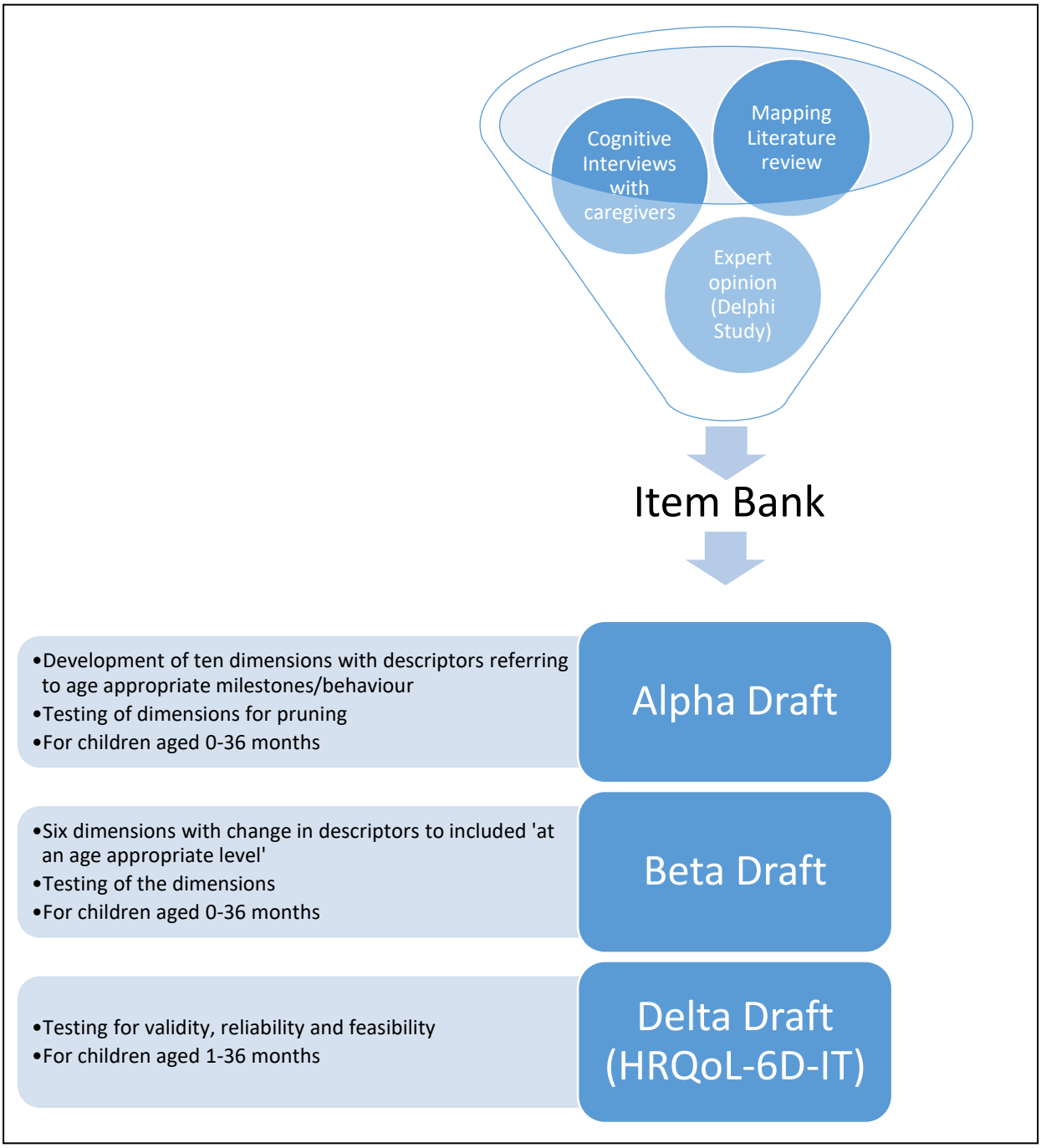


Figure 8-1 Procedure for the Development of the HRQoL-6D-IT

A mapping review of the literature identified fifteen HRQoL measures for children under the age of seven years (Chapter 3). Only five of these measures (HSCS-PS, PedsQL; DSQ, PROMIS PGH-7 and EQ-5D-Y Proxy) could be used to measure HRQoL in very young children (under three years of age). None of the measures performed well in the areas reviewed regarding the *a priori* set. The EQ-5D-Y and the PedsQL had the largest number of observable dimensions as per the ISPOR [13] and FDA guidelines [33]. The recall period of the PROMIS PGH-7 (7days) and the EQ-5D-Y (today) were the shortest and reduced recall bias [79] and measurement in an age group with great lability due to their rapid development [197]. The content validity of all five of the measures included a number of stakeholders and parents or children [79], [123], [175]. The EQ-5D-Y was the only measure which showed cross cultural validity in its development and included a LMIC, South Africa [145]. The HSCS-PS, PedsQL and DSQ relied on summary scores. The PROMIS PGH-7 had a scoring system developed with IRT and was linked to legacy measures to determine a utility score. The EQ-5D-Y proxy is currently under consideration for elicitation of utility scores. All measures showed sound psychometric properties. The EQ-5D-Y and PROMIS PGH-7 had the least number of items and thus the shortest completion time.There was the greatest need to develop a new instrument for the age group from 0-3 years. Due to the fact that the PedsQL had a comprehensive host of instruments across the age span it was not considered as a measure on which to model a new HRQoL measure. It was however, noted to be the most comprehensive measure currently available for very young children (three years and younger). The new measure would aim to improve on the content of the PedsQL with more observable dimensions, less items, shorter recall period and have a more psychometrically sound scoring system.

The EQ-5D-Y Proxy structure was considered as a good starting point for the development of a new measure. The structure was favourable as it was short in length with well-defined levels of report a simple recall period of 'today' and research was underway to assign preference weights to it. Furthermore the items included in its descriptive system were similar to items in all of the measures and included mobility/function, emotion, social and self-care. It had the advantage of being culturally appropriate for the South African context. All of the dimensions identified in the mapping review were included in the item bank for further testing and inclusion in the new measure.

Although the new instrument was developed with consideration of an existing measure, EQ-5D-Y Proxy, the accepted FDA and ISPOR guidelines for instrument development were followed [13], [33]. Generation of the item bank and age range for inclusion was multi-faceted and included: mapping review of generic HRQoL measures (Chapter 3), systematic review of preference based HRQoL measures, cognitive interviews with caregivers of children under the age of seven years (Chapter 4), a two round Delphi Study with experts in the field (Chapter 5) and a two day workshop with experts in the field. This process was followed to ensure content validity of the new instrument [13], [121]. The item generation further took into account

the conceptual framework of the adapted ICF model, which considers the traditional domains of the ICF as well as QoL and development across the lifespan. Review of the literature and cognitive interview identified a total of 42 items which were selected for inclusion in the item bank. This item bank was reduced to ten dimensions for testing on the Alpha Draft and six dimensions for testing on the Beta Draft.

A small pool of ten dimensions was tested on an Alpha Draft of the measure to inform which dimensions needed to be reduced and whether the dimensions could measure HRQoL across the identified age group (0-3 years) or if it was necessary to have different dimensions for different age groups. The Alpha Draft results showed that measurement across the age groups was a possibility if four of the dimensions were reduced and the descriptors were changed to include a reference of "at an age-appropriate level" as opposed to defining each of the age appropriate levels (Chapter 6).

These changes were captured on the Beta Draft for further testing. The Beta Draft of the questionnaire, which consisted of six items, performed better across the age groups but identified that the measure should only be used with children 1-36 months of age (Chapter 6).

The final questionnaire, HRQoL-6D-IT, was tested for validity and reliability on 187 caregivers of AI, CI and TD children (Chapter 7). In order to assess to what extent the new measure would meet the methodological requirements set out by Terwee (2011) the COSMIN checklist [350] was self-completed and can be seen in Table 8-1 below. This assisted with further identifying weaknesses and future research.

Table 8-1 Self-assessment of Research using COSMIN Checklist to Evaluate the HRQoL-6D-IT

(level of performance highlighted in grey)

Box General requirement for studies that applied Item Response Theory (IRT) Models				
	Excellent	**Good**	**Fair**	**Poor**
Was the IRT Model used adequately described? E.g. One Parameter Logistic Model, Partial Credit Model, Graded Response Model	IRT model adequately described	IRT model not adequately described		
Was the computer software package adequately described?	Software package adequately described	Software package not adequately described		
Was the method of estimation used adequately described? E.g. conditional maximum likelihood, marginal maximum likelihood	Method of estimation adequately described	Method of estimation not adequately described		
Were the assumptions for estimating parameters of the IRT model checked? E.g. unidimensionality, local	Assumptions of IRT model checked	Assumptions of IRT model partly checked	Assumptions of IRT model not checked or unknown	

independence, and item fit (e.g. differential item functioning)				
Box A. Internal Consistency				
Does the scale consist of effect indicators i.e. is it based on a reflective model?				
Design Requirements				
Was the percentage of missing items given?	Percentage of missing items described	Percentage of missing items NOT described		
Was the sample size included in the internal consistency analysis adequate?	Adequate sample size (≥100)	Good sample size (50-99)	Moderate sample size (30-49)	Small sample size (<30)
Was the unidimensionality of the scale checked? I.e. was factor analysis or IRT model applied?	Factor analysis performed in study population	Authors refer to another study in which factor analysis was performed in a similar study population	Authors refer to another study in which factor analysis was performed, but not in a similar study population	Factor analysis NOT performed and no reference to another study
Was the sample included in the unidimensionality analysis adequate?	7*#items and ≥100	5*#items and ≥100 or 6-7*#items but < 100	5*#items but <100	<5*#items
Was the internal consistency statistic calculated for each (unidimensional) (sub) scale separately?	Internal consistency statistic calculated for each subscale separately			Internal consistency statistic NOT calculated for each subscale separately
Were there any important flaws in the design or methods of the study?	No other important methodological flaws in the design or execution of the study		Other minor methodological flaws in the design or execution of the study	Other important methodological flaws in the design or execution of the study
Statistical methods				
For Classical Test Theory (CTT), continuous scores: was Cronbach's Alpha calculated>	Cronbach's alpha calculated		Only item-total correlations calculated	No Cronbach's alpha and no item-total correlations calculated
For CTT, dichotomous scores: Was Cronbach's alpha or KR-20 **calculated**?	Cronbach's alpha or KR-20 calculated		Only item-total correlations calculated	No Cronbach's alpha or KR-20 and no item-total correlations calculated
For IRT: Was a goodness of fit statistic at a global level calculated? E.g. x^2, reliability coefficient of estimated latent trait value (index of (subject or item) separation)				
Box B. Reliability: relative measures (including test-retest reliability, inter-rater reliability and intra-rater reliability)				
Only test-retest reliability tested				
Design Requirements				
Was the percentage of missing	Percentage of	Percentage of		

items given?	missing items described	missing items NOT described		
Was there a description of how missing items were handled?	Described how missing items were handled	Not described but it can be deduced how missing items were handled	Not clear how missing items were handled	
Was the sample size included in the analysis adequate?	Adequate sample size (≥100)	Good sample size (50-99)	Moderate sample size (30-49)	Small sample size (<30)
Were at least two measures available?	At least two measurements			Only one measurement
Was the administration independent?	Independent measurements	Assumable that the measurements were independent	Doubtful whether the measurements were independent	Measurement NOT independent
Was the time interval stated?	Time interval stated		Time interval NOT stated	
Were patients stable in the interim period on the construct to be measured?	Patients were stable (evidence provided)	Assumable that patients were stable	Unclear if patients were stable	Patients were NOT stable
Was the time interval appropriate?	Time interval appropriate		Doubtful whether time interval was appropriate	Time interval NOT appropriate
Statistical methods				
For Continuous scores: Was an Intraclass correlation coefficient (ICC) calculated?	ICC calculated and model or formula of the ICC described	ICC calculated but model or formula of the ICC not described or optimal. Pearson or Spearman correlation calculated with evidence provided that no systematic change has occurred	Pearson or Spearman correlation coefficient calculated WITHOUT evidence provided that no systematic change has occurred WITH evidence that systematic change has occurred	No ICC or Pearson or Spearman correlations calculated
For dichotomous/nominal/ordinal scores: Was kappa calculated?	Kappa calculated			Only percentage agreement calculated
For ordinal scores: Was a weighted kappa calculated?	Weighted Kappa Calculated		Unweighted Kappa calculated	Only percentage agreement calculated
For ordinal scores: Was the weighting scheme described? E.g. linear, quadratic	Weighting scheme described	Weighting scheme NOT described		
Box C. Measurement error: absolute measures				
NOT TESTED				
Box D Content Validity (including face validity)				
General requirements				
Was there an assessment of whether all items refer to relevant aspects of the constructs to be measured?	Assessed if all items refer to relevant aspects of the construct to be measured		Aspects of the construct to be measured poorly described AND this was not taken into consideration	NOT assessed if all items refer to relevant aspect of the construct to be measured.
Was there an assessment of whether all items are relevant	Assessed if all items are relevant	Purpose of the instrument was	NOT assessed if all items are relevant	

for the purpose of the measurement instrument? (discriminative, evaluative, and/or predictive)	for the purpose of the application	not described but assumed	for the purpose of the application	
Was there an assessment of whether all items together comprehensively reflect the construct to be measured?	Assessed if all items together comprehensively reflect the construct to be measured		No theoretical foundation of the construct and this was not taken into consideration	NOT assessed if all items together comprehensively reflect the construct to be measured
Were there any important flaws in the design or execution of the study	No other important methodological flaws in the design or execution of the study		Other minor methodological flaws in the design or execution of the study	Other important methodological flaws in the design or execution of the study
Box E Structural Validity				
Does the scale consist of effect indicators, i.e. is it based on a reflective model?				
Design Requirements				
Was the percentage of missing items given?	Percentage of missing items described	Percentage of missing items NOT described		
Was there a description of how missing items were handled?	Described how missing items were handled	Not described but it can be deduced how missing items were handled	Not clear how missing items were handled	
Was the sample size included in the analysis adequate?	7*#items and ≥100	5*#items and ≥100 or 5-7*#items but <100	5*#items but <100	<5*#items
Were there any important flaws in the design or methods of the study?	No other important methodological flaws in the design or execution of the study		Other minor methodological flaws in the design or execution of the study (e.g. rotation method not described)	Other important methodological flaws in the design or execution of the study (e.g. inappropriate rotation method)
Statistical methods				
For CTT: Was exploratory or confirmatory factor analysis performed?	Exploratory or confirmatory factor analysis performed and type of factor analysis appropriate in view of existing information	Exploratory factor analysis performed while confirmatory would have been more appropriate		No Exploratory or confirmatory factor analysis performed
For IRT: Were IRT test for determining the (uni-) dimensionality of items performed?	IRT test for determining (uni)dimensionality performed			IRT test for determining (uni)dimensionality NOT performed
Box F: Hypothesis Testing				
Was the percentage of missing items given?	Percentage of missing items described	Percentage of missing items NOT described		
Was there a description of how	Described how	Not described but	Not clear how	

missing items were handled?	missing items were handled	it can be deduced how missing items were handled	missing items were handled	
Was the sample size included in the analysis adequate?	Adequate sample size (≥100 per analysis)	Good sample size (50-99 per analysis)	Moderate sample size (30-49 per analysis)	Small sample (<30 per analysis)
Were hypotheses regarding correlations or mean differences formulated a priori (i.e. before data collection)?	Multiple hypotheses formulated a priori	Minimal number of hypotheses formulated a priori	Hypotheses vague or not formulated but possible to deduce what was expected	Unclear what was expected
Was the expected direction of correlations or mean differences included in the hypotheses?	Expected direction of the correlations or differences stated	Expected direction of the correlations NOT stated		
Was the expected absolute or relative magnitude of correlations or mean differences included in the hypotheses?	Expected magnitude of the correlations or differences stated	Expected magnitude of the correlations or differences NOT stated		
For convergent validity: Was an adequate description provided for the comparator instrument(s)?	Adequate description of the constructs measured by the comparator instrument(s)	Adequate description of most of the constructs measured by the comparator instrument(s)	Poor description of the constructs measured by the comparator instrument(s)	NO description of the constructs of the comparator instruments(s)
For convergent validity: When the measurement properties of the comparator instrument(s) adequately described?	Adequate measurement properties of the comparator instrument(s) in a population similar to the study population	Adequate measurement properties of the comparator instrument(s) but not sure if these apply to the study population	Some information on measurement properties (or a reference to a study on measurement properties) of the comparator instrument(s) in any study population	No information on the measurement properties of the comparator instrument(s)
Were there any important flaws in the design or methods of the study?	No other important methodological flaws in the design or execution of the study		Other minor methodological flaws in the design or execution of the study (e.g. rotation method not described)	Other important methodological flaws in the design or execution of the study (e.g. inappropriate rotation method)
Statistical methods				
Were design and statistical methods adequate for the hypotheses to be tested?	Statistical methods applied appropriate	Assumable that statistical methods were appropriate e.g. Pearson correlations applied, but distribution of scores or mean (SD) not presented	Statistical methods applied NOT optimal	Statistical methods applied NOT appropriate

Box G: Cross-cultural validity				
NOT TESTED				
Box H: Criterion Validity				
Design requirements				
Was the percentage of missing items given?	Percentage of missing items described	Percentage of missing items NOT described		
Was there a description of how missing items were handled?	Described how missing items were handled	Not described but it can be deduced how missing items were handled	Not clear how missing items were handled	
Was the sample size included in the analysis adequate?	Adequate sample size (≥100)	Good sample size (50-99)	Moderate sample size (30-49)	Small sample (<30)
Can the criterion used or employed be considered as a reasonable 'gold standard'	Criterion used can be considered an adequate 'gold standard' (evidence provided)	No evidence provided, but assumable that the criterion used can be considered an adequate 'gold standard'	Unclear whether the criterion used can be considered an adequate 'gold standard'	Criterion used can NOT be considered an adequate 'gold standard'
Were there any important flaws in the design or methods of the study?	No other important methodological flaws in the design or execution of the study		Other minor methodological flaws in the design or execution of the study	Other important methodological flaws in the design or execution of the study
Statistical Methods				
For continuous scores: Were correlations, or the area under the receiver operating curve calculated?	Correlations or AUC calculated			Correlations or AUC NOT calculated
For dichotomous scores: Were sensitivity and specificity determined?	Sensitivity and specificity calculated			Sensitivity and specificity NOT calculated
Box I: Responsiveness				
NOT TESTED				

IRT Analysis

IRT analysis was used primarily in this research to assess the performance of each dimension in terms of item characteristic curves, item information curves and category characteristic curves which were used to compliment the data obtained from classical test theory. Classical test theory was used in addition to IRT to test for internal consistency and item-rest correlation. Unidimensionality and The IRT analysis scored poorly according to COSMIN as neither the model of IRT nor the methods of estimation were described. The model of IRT can however be assumed as a graded response model as the data was ordinal and category characteristic curves were generated. The assumption for estimating parameters of the IRT model (unidimensionality) was not checked using the recommended differential item functioning but rather with classical test theory of Factor Analysis.

Internal Consistency

Factor Analysis results revealed two distinct subscales of: 1) activity and participation and 2) body functions. The emergence of these two sub-scales was strengthened by the fact that the dimensions of pain and eating, which formed the subscale of body functions, were shown to increase reliability if removed. A lot of problems in these two dimensions were further indicative of illness. The internal consistency of the overall scale was good α=0.83 [176]. A weakness according to the COSMIN guidelines was that internal consistency was not calculated for the two subscales separately [350], [351].

Reliability

A notable weakness of the HRQoL-6D-IT was that only test-retest reliability was assessed and neither inter-rater nor intra-rater reliability was tested. The test-retest performed poorly overall according to the COSMIN checklist with a small sample size for test-retest of <30 participants [350], [352]. The sample size of 19 was calculated according to a Pearson's correlation co-efficient of 0.6. According to the COSMIN guidelines this calculation should have been performed with a weighted Kappa as Spearman and Pearson's correlation coefficients do not take systematic error into account [352]. Due to the limited variance in the TD group of children the test-retest was evaluated on percentage of agreement was calculated which is further criticized by Mokkink et al (2012) as "it does not correct for chance of agreement" [352] page 27. A further weakness included the fact that no measurement was taken to indicate stability of the participant's health over the week between the two measurements. The time period between assessments is not specified in the COSMIN checklist as it is dependent on the measurement [352]. It was suggested that a time period of about two weeks could be considered [352]. The inclusion of children with chronic, stable illness is recommended in future testing to allow greater variance in the scores and better assessment with weighted kappa.

Measurement Error

Measurement error was not assessed in the testing of the HRQoL-6D-IT as only one measurement was taken for all participants except for the few who had a repeat measure to assess test-retest. No children with chronic or acute illness were included in the group who had a repeat measure thus limiting the test-retest results and further limiting the calculation of measurement error or minimal important change. The study design of future research should allow for measurement error to be calculated as it assesses the random error which occurs in the participant's HRQoL-6D-IT score that cannot attributed to change in health condition [350], [352]. Minimal important change would indicate whether the HRQoL-6D-IT is sensitive in detecting the smallest important change in the participant's health condition [350], [352].

Content Validity

The procedure followed for establishing content validity were in line with the ISPOR recommendations [13]. The process was rigorous and included a narrative and mapping review, the view of caregivers was sought in the cognitive interviews and expert opinion was assimilated in the Delphi study. Although the number of participants who participated in the Delphi study was less than anticipated it was still within the recommended guideline of participants to reach a consensus [249]. The theoretical foundation [350] for the HRQoL-6D-IT was based on the measurement of HRQoL with dimensions representative of the theoretical model of the ICF. The content coverage of the items and the domain descriptors [351] were informed by all both caregivers and experts in the field. This was further modified according to results from testing of the preliminary instruments. The item bank which was developed and pruned during these steps was tested with caregivers of children in the Alpha Draft of the instrument. As further pruning of dimensions was necessary a Beta Draft was developed and tested with caregivers of children. Although this process was limited to English speaking individuals it did gather the input from a number of caregivers and experts from different cultural backgrounds.

Structural Validity

The structure of the HRQoL-6D-IT was tested using rotated factor analysis. The structure of the instrument was further strengthened with the testing and reduction of items in the Alpha and Beta Draft with classical test theory, including factor analysis, and IRT.

Hypothesis Testing

The hypotheses that were formulated lacked specificity in terms of the magnitude of the correlation between the HRQoL-6D-IT and the other measures. Furthermore the direction and magnitude of the relationship between results of the HRQoL-6D-IT and other variables was not adequately stated. Hypotheses were generated based on results from other HRQoL measures, mostly for older children, such as the EQ-5D-Y. The comparator instruments were well described and reference to other studies was given. Furthermore, the statistical tests for convergent validity were appropriate.

Criterion Validity

According to Mokkink et al (2012) state in their guidelines that as no golden standards exist for HRQoL measures, the use of reference measures should be considered as reasonable [352]. The ASQ is well validated and extensively used as a parent/caregiver proxy report measure. The FLACC and NIPS are both validated and extensively used in the clinical field however their use with caregivers for proxy completion is not as well established. This may have led to the lower correlations between the pain scores when compared to the other dimensions. There was no appropriate comparator instrument for the dimension of

eating on the HRQoL-6D-IT. A self-designed instrument capturing a proxy report of the child's diet history was used. The self-report instrument performed well and there was a moderate correlation with a Kappa score of 0.6.

Cross-Cultural Validity and Responsiveness

Neither the cross-cultural validity nor the responsiveness was tested on the HRQoL-6D-IT. These are both highlighted as recommendations for future research. According to the COSMIN guidelines at least two measures need to be taken in a longitudinal study design to assess responsiveness [352]. Participants should include a mix of those who are likely to improve and deteriorate. This mix of participants helps to determine whether no change in the results is a reflection of patient change or a due to measurement error on the instrument [352]. Measurement of the participant's change needs to be taken on a global rating scale or similar measure [352]. Cross-cultural validity needs to be tested in different language and cultural groups. COSMIN recommends forward-backward translation with a minimum of two translators [352]. The translated instrument should be pre-tested for interpretation and relevance before validity testing commences. The participants recruited for cross-cultural validity testing should be similar, in terms of age, gender and medical condition, to those on the original instrument testing to ensure that testing is limited to difference in culture only [352].

In conclusion, the HRQoL-6D-IT performed as anticipated with acceptable known group construct validity in that it highlighted differences in HRQoL with AI being ranked with a lower rating of general health than CI and TD children. The concurrent validity of the scale was acceptable with fair to moderate correlation with appropriate items from other validated instruments such as the ASQ, FLACC and NIPS. In addition, caregivers were able to reliably report on HRQoL of their very young children. The instrument development was limited to the South-African English speaking population and subsequently limited its cross-cultural relevance. The inclusion of TD children improved the validity of the instrument as it ensured that the sample was more culturally represented and did not only include the population of caregivers accessing public health care services. There is evidence to suggest that the HRQoL-6D-IT is valid and reliable for use with children aged 1-36 months with English speaking caregivers in South Africa. It is however, recommended that future studies with a larger sample size and with different cultural groups be conducted to confirm these results

8.1.1 Study Limitations

Use of English caregivers throughout the study is a limitation as it excluded the many Xhosa and Afrikaans speaking caregivers who could have contributed different data. Furthermore, the application of the instrument is currently limited to English speaking individuals and will need to be forward-backward translated into the official languages of South Africa and tested for validity and reliability. The inclusion of the day-care centres led to the inclusion of a more educated group of caregivers in the TD group. Thus, the results may be biased toward middle class respondents.

None of the contextual information collected included SES of the caregiver which limited the results. Furthermore, education level of the caregiver was only sought in the cognitive interviews and could further have informed the results of the other chapters. The participant selection for the Delphi study was limited to experts that were known to the research group. This introduced selection bias which was further compounded by the fact that there were no representatives from education or social work on the panel of experts. Furthermore, the sample size for both rounds of the Delphi study was small.

There were small numbers of children represented in each age group in testing of both the Alpha and Beta Drafts of the instrument which could have confounded the results. The dimensions of eating and pain had a high frequency of report of some problems in TD children when compared to the other dimensions. It may be necessary to test different levels of report for these questions in the future. Test-retest reliability was not satisfactorily established in this study due to the limited variance in the dimensions scores for TD children. All research conducted was of a cross-sectional nature, except for the test-retest reliability, which could limit the interpretation of the results. Longitudinal study design could have better explained the responsiveness of the measure and given clearer results pertaining to the relationship between the caregiver health and their child's perceived health.

8.1.2 Recommendations for Practice

The results from this study showed that it performed well in a South African context in measuring HRQoL in both AI and CI children attending a children's hospital as it discriminated well between ill and 'healthy' children. Although the initial development of the HRQoL-6D- IT is an important step towards producing a definitive instrument to measure HRQoL in very young children, the limitations listed above imply that further work needs to be done to validate the instrument in different contexts and different populations. It is thus premature to suggest that the HRQoL-6D- IT be used as a stand-alone outcome measure. Instead it is recommended that the HRQoL-6D-IT be included as an addition to standard patient (proxy) reported

outcome measures in routine clinical practice and research studies within South Africa to assist in further establishing its validity and reliability. The Paretian Classification of Health Change, a scoring system developed for the UKs NHS for the EQ-5D, could be considered for the scoring of the HRQoL-6D-IT in the clinical setting to monitor progress [353]. This scoring system describes the dimension scores as: overall health improvement (when one dimension has improved with no change in the other dimensions)or overall worsening of health(when one dimension has worsened and there was no improvement in the other dimensions) [353].

8.1.3 Recommendations for Research

It is recommended that future research be done on the measure to assess the feasibility and clinical utility of the measure. Future research should include additional demographic information which could account for reporting of HRQoL such as socio-economic status and number of caregiving hours the caregiver spends with the child. The inclusion of factors relating to the caregiver's health and their reasoning behind reporting problems would clarify the interaction between child and caregiver health. Study designs to collect longitudinal data should be considered to determine the performance of known groups over time, the responsiveness of the measure and collect reliability data. Collecting data regarding the severity of the health condition would assist in establishing the sensitivity of the measure.

Incorporating the measure as a routine outcome measure in clinical practice could enhance the holistic management of patients. Determining the responsiveness of the measure to change in health over time would further strengthen the measurement properties of the HRQoL-6D-IT. Future development including international input would greatly enhance the cross-cultural acceptability and validity of the measure. Translation and validation of the instrument in the other ten official languages of South Africa would improve its value and use within South Africa.

The development of a scoring system for the descriptive system using IRT analysis would greatly enhance the analysis of the results from the descriptive system and comparing HRQoL across groups. The development of preference-based weights for use on HRQoL-6D-IT health states would be beneficial for CUA in this very young age group. In the interim dimension scores could be described using the Paretian Classification of Health Change scoring system [353].

8.1.4 Recommendations for Policy

The measurement of HRQoL across the population of South Africa should be considered. At minimum there is a need to monitor the HRQoL of the most vulnerable of society, the young children living in poverty. The EQ-5D has been used successfully in a population health study in both China and Sweden where the average level of population health and its distribution has informed health policy [354]–[356]. Measurement of HRQoL in the very young child should be considered very carefully due to the potential benefits of improving care of this vulnerable age group by improving the measure of HRQoL and the impact of interventions aimed at this age group. It could further improve clinical practice with clinicians considering this patient group more holistically. If preference based scoring is developed, CUA will become more feasible and possibly lead to a more rational allocation of resources.

HRQoL is important to caregivers and their children and it is incumbent that health professionals take caregiver views into account during the management of children and their health. Furthermore, we need to ensure that resources are allocated rationally to maximise the health of the youngest and most vulnerable of our population. Consideration should be given to the words of Nelson Mandela “Children are our greatest treasure. They are our future” [357].

In my journey towards the development of the HRQoL-6D- IT I was struck by the caregivers’ deep commitment to and concern with the health and well-being of their children. By including their perceptions of the HRQoL of their children in decision making, health professionals can ensure that their interventions are both child and family centred. A worthy goal!

9 References

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10 Appendices

10.1 Appendix 1 Generic Health-Related Quality of Life Measures

Table 10-1 Descriptive Properties of Generic HRQoL Measures

Instrument	Age range (years)	Development Procedure	Dimensions	Completion	Questionnaire Format	Items	Recall period	Referenced: self/others	Reference
HUI:2 **HUI:3**	5-8	*Product of more than 30 years of research. *Developed in Canada. *Evolution guided by theoretical and empirical evidence. * Classification system is designed to link directly with preference-based scoring. *HUI: 1 was developed to evaluate outcomes of infants with very-low birth-weight. *HUI: 2 used the core set from HUI: 1 to assess the burden of childhood cancer but has since been applied to various groups. *HUI: 3 was developed from HUI: 2 with greater applicability in both clinical and general population studies as well as having structural independence among attributes.	1.Sensation 2.Mobility 3.Emotion 4.Cognition 5.Self-Care 6.Pain (7.Fertility) 1.Vision 2.Hearing 3.Speech 4.Ambulation 5.Dexterity 6.Emotion 7.Cognition 8.Pain	Proxy (Proxy viewpoint)	Likert-type scale (Quality with 3-6 levels of report)	15/40	Current or Past week or Past 2 weeks or Past 3 weeks	Referenced against children of the same age.	[177] [178] [178] [199]

HSCS-PS	2,5 – 5	Derived from HUI Mark II & III * Developed in Canada and Australia *Selection of Dimensions from HUI Mark II & III *Defining levels of report * Content Validation and consensus * Development of clinician and parent Questionnaires and field testing. * Testing	1.Emotion 2.Hearing 3.Speech 4.Ambulation 5.Dexterity 6.Learning & Remembering 7.Thinking & problem solving 8.Pain 9.Behaviour 9.General health 10.Self-care 11.Vision	Proxy (Proxy viewpoint)	Likert-type Scale (Quality with 4 levels of report)	12	Not specified	Referenced to children of same age with four of the questions.	[174]
PedsQL 4.0	1-12 months 13-24 months 2-4 5-7	*Derived from a USA cancer database (PCQL) and used as a generic measure across the paediatric population. *PCQL based on extensive literature review, open-ended interviews with patients and their family, discussion with health-care providers. Followed by instrument development and testing. Changes were made and further testing undertaken until development of and testing of the third and final instrument. *The infant scale was developed with the same theoretical framework. *A literature review and consultation with health care professionals formed the groundwork. * Parent focus groups and cognitive interviews. *Pre-testing and field testing of the new infant scale.	1.Physical Health 3.Emotional Function 4.Social Function 5.School Function	Proxy Proxy Proxy Proxy/self (Proxy view point)	Likert-type Scale (Frequency with 4 levels of report)	36 45 15/23 15/23	1 month	Self-referenced.	[200] [73] [202] [201]

WCHMP	0-5	*Developed in the UK *Open ended questions to parents exploring the understanding of concepts. *Answers categorised *Modifications made to dimensions improving comprehensibility and acceptability.	1.General Health 2.Acute Minor Illness 3.Behavioural 4.Accident status 5.Acute significant illness 6.Hospital admission 7.Immunization 8.Chronic illness 9.Functional health 10.HRQoL	Proxy (Proxy view point)	Mixed model questionnaire including Likert-type and open questions. (Mixed Likert scale: Including frequency scale and quantity scale).	16	3/10 questions specify recall period of the last year. The other questions have no specified recall period.	One question referenced to other children. Remaining questions self-referenced.	[358] [203]
DCGM	4-7	*Concurrent development between researchers of seven European Countries. *Literature Review *Focus Groups *Generation of Items *Translation *Pilot testing	1. Mental 2.Social 3.Physical	Proxy (View point of the child)	Likert-type Scale (Frequency scale with 5 levels of report)	37 12	Last Four weeks	Referenced to self	[29] [30] [359]
DSQ	4-7	*Developed from DCGM *Focus groups with parents of children aged 4-7 *Item selection *Research on use of smileys guided layout of Questionnaire *Pilot testing *Item reduction *Testing Take 6 Scale	1.Mental 2.Social 3.Physical	Assisted-report and Proxy (view point of the child)	Likert-type Scale (Quality scale with pictorial smiley faces and five levels of report)	12 6	Not specified	Referenced to self	[206]
TAPQOL	1-5	* Developed in the Netherlands. *Review of literature and existing questionnaires and discussion with HRQoL experts. *Consideration of Sub-dimensions *Consideration of Dimensions	1.Physical 2.Social 3.Cognitive 4.Emotional	Proxy (Proxy view point)	Likert-type Scale (Frequency scale with 3 levels of report.	43	3 months	Referenced to self	[207] [208] [360]

		*Preliminary Questionnaire *Feasibility testing of preliminary Questionnaire. * Deletion or paraphrasing of Questionnaire. * Final TAPQOL Questionnaire			Followed by a Quality scale with 4 levels of report for 5 of 8 sections)				
CHQ	5-18 years	*Developed in the USA *Review of literature and existing scales as well as previous measurement experience guided identification of core concepts. *Initial CHQ constructed and tested on parents and children. *Data from initial evaluation study informed inclusion of items. *Varying lengths of the form was constructed.	1. Physical functioning 2. Role Functioning: emotional 3. Role functioning: behaviour 4. Role Functioning: Physical 5.Bodily Pain 6. General Behaviour 7. Mental Health 8. Self-esteem 9.General Health Perceptions 10. Parental Impact: Time 11. Parent Impact: Emotional 12. Family Activities 13. Family Cohesion 14. Change in Health	Proxy (Proxy view point)	Mixed Likert-type Scale (Frequency, Quality and Likelihood scales with 4-6 levels of response type of scale)	28 50	4 week recall except for 3 dimensions (change in health and family cohesion – general. General Health- past/current and future)	Referenced to both self and others	[59] [60]

ITQOL	2 months – 5 years	*Developed in the USA *Adoption of WHO definition of health. *Review of infant health literature and developmental guidelines. *Reduction of items for a short form included: factor analysis, stepwise regression and multi-trait item-scaling analysis.	1.Overall health 2.Physical abilities 3.Growth and Development 4.Pain 5.Temperament and Moods 6.Behaviour 7.Getting along 8.General Health 9.Perceptions 10.Change in Health 11.Impact-Emotional 12.Impact-Time 13.Family Cohesion	Proxy (Proxy view point)	Likert-type scale (5 levels of report type of scale not specified)	97 47	Current, past and future (varying for each question)	Mostly self reference. Referenced to children of the same age with behaviour and health question.	[210] [211] [362]
Kiddy-KINDL^{R}	4-6 3-6	*Developed in Germany *Derived from KINDL-R where they interviewed children on the components of QoL. * Thereafter they did a pilot study and a 3 year observational study on the KINDL-R. *Development of the Kiddy KINDL^{R} is not clear.	1.Physical 2.Emotional 3.Self-Esteem 4.Family 5.Friends 6.Everyday Functioning 7.Additional disease module	Self Proxy (both with face-to-face interview) (Proxy viewpoint)	Likert-type Scale (Frequency scale with 3 levels for self-report and 5 levels for proxy)	12 - self 47 - proxy	Not specified	Referenced to self.	[212]
C-QOL	5-8	*Developed for use in Thailand. *WHOQOL facet definitions were examined for suitability to children and language simplified as necessary. * Alterations made to facets according to suitability in childhood life and other facets omitted.	1.Physical 2.Psychological 3.Independence 4.Social relationships 5.Environment 6.Religion	Self-report Proxy-report (Proxy view point)	Mixed Likert-type Scale with pictorial classification.	54	Not specified	Referenced to self.	[213] [214]

		*WHOQOL construct examined by focus groups interviews. * Children's ability to answer 5 point Likert-type scale was examined. * Two sets of questionnaires developed and tested for psychometric properties.	7.Child's Rights						
PROMIS PGH-7	5-17	*Developed in the USA *Dimension Content Specification including content expert input; child and parent interviews and Literature Review *Existing Item classification; New item creation and Item writing. *First Item pool tested in cognitive interviews; translatability review and reading level analysis. *Second item pool created *Testing of questionnaire *Final Questionnaire *reviewed by panel of experts for proxy completion. *Content was not altered but wording was changed *Proxy-cognitive Interviewing * Test Forms Developed and tested	1.Physical Function 2.Emotional 3.Peer 4.Relationships 5.Fatigue 6.Pain 7.Interference	Proxy-report (Proxy view point)	Likert-type scale (Quality Scale with 5 levels of report)	7	7 day	Referenced to self.	[151] [152] [153] [215] [154]
TEDQoL	3-8	*Developed in the UK *Interviews with children using two teddy bears. * Teddy Bears would identify themselves with one representative of the positive side and one of the negative side asking the child to identify with one of the Teddy bears. * After identifying with a bear they were asked to point to a picture showing how happy or sad they were about the trait.	1.Physical Competence 2.Peer Acceptance 3.Maternal Acceptance 4.Psychological Functioning 5.Cognitive Functioning	self	Dichotomous And Likert-type scale (Quantity scale with 4 levels of report)	23	Not specified	Referenced to self.	[216]

		* Children scored on an ability and happiness score. * Follow up study explored having two bears but no happiness question but rather a Likert-type scale of how accurate they represent the bear.							
FS II(R)	0-9 months 10 months – 2yrs 2-5yrs 5-11yrs	*Developed in the USA *Literature review * Knowledge from clinical experience together with interviews with mothers led to the development of an item pool. * The instruments was reviewed by panel of experts for content, clarity and relevance to the constructs to be measured. *FSI was created and pretested. * Necessary changes were made and the FSI was tested for psychometric rigour. * The FS I was modified to form the FS II(R) on the basis of findings from psychometric testing.	1.Communication 2. Mobility 3.Mood 4.Energy 5. Sleeping 6. Eating 7. Toileting Patterns.	Proxy interview (Proxy view point)	Likert-type (First Question for each dimension is on a Frequency scale and the second question for each dimension is on a Likelihood scale)	43 14	Two weeks	Referenced to self.	[44] [45]
EQ-5D-Y proxy	4-18	*Derived from the adult version, EQ-5D, to enable young respondents to self-report. *International team of experts reviewed the EQ-5D dimension definitions and adapted them to be more applicable to the younger age group. *The wording of the questionnaire was revised for improved comprehension. *Translation of the tool for multi-national cognitive interviews. *Cognitive interviews were carried out with healthy and cognitively ill children from 4 European countries.	1.Mobility 2.Self care 3.Usual Activities 4.Pain/Discomfort 5. Worried, sad, unhappy	Proxy (Proxy view point or view point of child)	Likert-type scale (Quantity with 3 levels of report) Rating of Health on VAS	5 (+ rating of health on VAS)	Today	Referenced to self.	[144] [145]

		*Integration of results from cognitive interviews into a provisional new tool – EQ-5D-Y. *Comparison of results between EQ-5D and EQ-5D-Y. *Psychometric testing. *Rewording of the instrument for proxy use in children 4-18 years of age.							

Table 10-2 Psychometric Properties of the Generic HRQoL Measures

Instrument	Validity				Reliability			Practicality	Score	Reference
	Criterion Validity	Construct Validity	Face Validity	Content Validity	Internal consistency	Inter-rater reliability	Test-Retest Reliability			
HUI:2 & HUI:3	Subsequent to its development used as a 'gold standard' for other HRQoL measures.	**Convergent Validity** 1.HRQoL on the day before admission for acute illness and the day of admission was shown to be mutually exclusive. 2. There was a significant correlation between the degree of functional limitation on measure compared to medical consumption. **Discriminant Validity** Mobility and cognition contrasted with clinical entities (Scoliosis and Mental	Developed from research and data collected from previous versions of the measure.	Developed from more than 30 years of research from theoretical and empirical evidence.		Inter-rater reliability was high as measured by Spearman, Pearson and Inter-class correlation coefficients with the lowest results in the emotional dimension.		No missing data. 10-15 minutes completion time. Cost: $5000	Utility Score	[177] [178] [223] [363] [228]

		Retardation). Discriminative power was shown for both.								
HSCS-PS	Strong relationship between specific dimensions of the HSCS-PS and the following measures: Bayley Scales of Infant Development; Vinelands Adaptive Behavior scales; The Teller Visual Acuity Test and Gross Motor Function Classification System.	**Convergent Validity** Correlation between GMFCS and mobility dimension was excellent. Correlation between GMFCS and dimensions of self-care; dexterity; speech and thinking & problem solving was moderate to good. Correlation between GMFCS and dimensions of learning& remembering; vision; pain & discomfort were poor. Very low birth weight is a determinant of the proportion of children with multiple dimensions of health affected.	Field testing of the pilot version of the instrument to make necessary changes.	Developed from a series of studies on the development, expansion and refinement of the HUI Draft system was tested on over 80 children by developmental paediatricians and neonatologists with qualitative feedback.		Inter-rater reliability (between proxy- & clinician-report) Moderate with kappa's ranging from 0.47- 0.66 for each dimension.	Moderate to excellent kappa's ranging from 0.51-1.00. for each dimension.	Less than 10 minutes completion time. Grade 8 literacy level. Acceptable to parents. Cost: Free of Charge.	None	[174]

PedsQL 4.0	There was a medium to large correlation with parent-report PedsQL and their extent to which their child's HRQOL interfered with their daily routine and concentration at work. Parent-child agreement showed intra-class correlations to have moderate to good agreement. **<u>Infant Scale</u>** 41 of 45 items loaded at least 0.40 on their	**Convergent Validity** There was a small to medium correlation between PedsQL self –report scales and indicators of morbidity and burden of illness (seeking medical care in 30 days and number of days missed). **Discriminant Validity** Healthy children had higher scores than acutely or chronically ill children. **<u>Infant Scale</u>** Discriminant Validity Parents of infants with acute health conditions report statistically significant lower HRQoL score for their infants than parent of health infants.	Field testing was done before the final testing of the instrument. **<u>Infant Scale</u>** Field testing was done before the final testing of the instrument.	Initially derived from a cancer database and further evolved from 15 years of research. Constructs modified from previous versions of the measure. The items on measures for different ages and completion differ only in age appropriate language use and tense. **<u>Infant Scale</u>** Parent focus groups and cognitive interviews conducted for infant scale.	α≥0.70 (internal consistency) α approaching 0.90 for total scale for proxy- and self-report. **<u>Infant Scale</u>** Internal consistency All scales and summary scales >0.7 and total score >0.9			Completion in approximately 5 minutes. Missing Responses Self-report 1.2 -1.54% Proxy-report 1.95% Flesch-Kincaid readability score ranged from first to third grades. Cost: Free of charge **<u>Infant Scale</u>** Feasibility 0.7% of missing items	Summary Score	[200] [364] [365] [366] [367] [202] [201]

	hypothesized factor. Suggesting that the data were generally consistent with the a *priori* hypothesized five-factor model.									
WCHMP	Parent reporting was highly correlated with health records. Kw 0.824 - 0.987. Comparison between medical judgement between two paediatricians were good from Kw 0.770 – 0.949. Comparison between medical judgement between	**Convergent Validity** Relationships between variables occurred more frequently than expected by chance at the 95% confidence level. Further, adverse outcomes at 8 weeks was associated with an increased risk of the same outcome at 8 months.			Ranging from 0.547 – 0.859.	Inter-rater reliability good Kw 0.760 – 1.0.	Test-retest Reliability was good for four dimension and moderate in the remaining dimensions.	Maximum 10 minutes to complete. Cost: Free of charge.		[203] [358]

	parent and paediatrician was good from Kw 0.696 – 0.949.									
DCGM	Moderately correlated with FSII-R and KINDL, PedsQL, VSP-A.	**Discriminant Validity (37 items)** Girls and older adolescents reported lower emotional well-being than boys and younger children. Children with lower levels of affluence had worse HRQoL than other children. Children with severe health conditions had worse HRQoL than other children in all dimensions. *Results reported for self and proxy completion for children >8 years of age.*	Field testing was carried out before testing of instrument.	Generation of items based on literature review and focus groups in seven European countries.	Best used in combination with KIDSCREEN measure to compare date epidemiologically referenced data. KIDSCREEN measures are only available for children aged 8-18 years.		Test-retest reliability ICC (37 items) ranging 0.71 - 0.83. Paired T-test showed no significant difference. *Results reported for self and proxy completion for children >8 years of age.*	(37 items) Missing answers <5% Cost: €60 *Results reported for self and proxy completion for children >8 years of age.*	Summary Score	[359] [368] [204] [206]
DSQ	Moderate convergent validity to proxy	**Discriminant Validity** The HRQoL decreases as the	Pilot testing of instrument before final instrument was	Developed from validated DCGM with	α=0.64 (child version) α=0.71 (proxy-report)		Test-retest ICC = 0.69.	Child-friendly wording, concepts and layout.	Summary Score	[206]

	completion of General Health Profile; CHQ and KINDL^{R}.	severity of illness increases. There is also a difference between medical conditions and HRQoL.	tested.	additional focus groups with parents of children aged 4-7 years.	Gutmansplit-half reliability 0.72 (child version) and 0.71 (proxy-report).			2-5 minute interviewer administered completion. Cost: €60		
TAPQOL	Kaiser-Meyer-Olkin Measure of sampling adequacy 0.795 Bartlett's test of sphericity <0.4. HOMALS indicated that the category quantification for 38/43 items did not violate the assumed ordinality. Spearman's correlation coefficients between TAPQOL and FS-II(R) 0.52-0.54.	**Discriminant Validity** 1.Comparison between preterm and term children With preterm children having lower mean rank score. 2. Children with good health and less good health with children with good health having a higher mean rank score. 3. Healthy children and children with chronic disease with children with chronic disease having a lower rank mean score. 4. Scales differentiated between healthy and less healthy groups of children.	Pilot testing of instrument before final instrument was tested.	Review of existing questionnaires, literature and discussion with HRQoL experts.	Internal consistency ranging from α0.66 – 0.90. Overall Reliability α≥0.70.			Response rate 83 - 95% Missing answers 1-5% Non-unique answers 1% Cost:€32 for the manual		[360] [207] [369] [322] [370] [371] [208]

CHQ	Items and concepts were compared to other published data and measures. Norms were obtained for CHQ and provided frame of reference for interpretation absence of 'gold standard.'	Confirmation of expected hypothesis: - Mean scores highest for healthy sample. -General health scores – lowest for severely ill children. -Physical function scores were lowest in children with Juvenile Idiopathic Arthritis. -Lower mean scores for ADHD in psychosocial dimensions.	Initial CHQ was pilot tested on parents and children for their input.	Confirmation of conceptual framework was evaluated using factor analysis. Factor analysis studies identified patterns of correlation between scales interpreted as 'physical' and 'psychosocial'. Physical & psychosocial accounted for 59.2% of total measured variance.	CHQPF 50 α≥0.70. Physical sub-scale α=0.93. Psychosocial sub-scale α=0.93. CHQPF 28 ≥0.74. Physical sub-scale α=0.89. Psychosocial sub-scale α=0.89.			Flesch-Kincaid Readability: CHQPF 28-Grade 3.2. CHQPF50 – Grade 3.5. Cost calculated according to study design.	Summary Score	[59] [60] [363]
ITQOL	Good Correlation with TAPQOL.	**Discriminant Validity** Good discrimination between healthy children and those with parent reported chronic conditions.		Adopted WHO definition of health for development. Conceptually similar to the CHQ.	**97 item measure** α>0.70. **47item measure** α>0.77.		Test retest ICC≥0.50; p<0.01	Response rate >80%. <2% missing and non-unique answers. Cost calculated according to	Unknown	[36] [75] [35] [36] [61]

		Good discrimination between children with and without diagnosed respiratory disease Babies in NICU recorded lower HRQoL scores than healthy babies. 91-100%scaling success for short form						study design.		
Kiddy – KINDL^R	Correlated with CHQ; SF-36 and Life-Satisfaction. *No psychometric data available for Kiddy-KINDL^R, the above is reported for KID- and KIDDO-KINDL^R.*	**Discriminant Validity** Able to distinguish differences in HRQoL in children with different diseases. *No psychometric data available for Kiddy-KINDL^R, the above is reported for KID- and KIDDO-KINDL^R.*		**Item-Analysis** Using Multi-trait Analysis Programme (scale fit) above 80% for all sub-scales.	Cronbach's α reached values around α=0.70 for most scales with ICC α>0.80 *No psychometric data available for Kiddy-KINDL^R, the above is reported for KID- and KIDDO-KINDL^R.*			Face to Face interview. 5-15 minutes for completion. Cost: Free.	Summary score	[212]
C-QoL	Multiple regression analysis showed all variables except the	**Discriminant Validity** Sick children obtained lower scores than healthy children in	Three Thai adult and children were asked to read the measure and comment	Modified from WHOQOL measure through focus groups	**Internal Consistency** Self-report α=0.86 proxy report α=0.84.		**Test-retest** Pearson correlation coefficien	Self-report. 30 minutes to complete. Cost: Not	None	[213] [214]

	children's acute/chronic (n=28) illness were associated with QoL, the represented sample was however very low. Father's income was the best single predictor of QoL. Other factors that had an impact on QoL were father's level of education, accommodation and travel to school.	facets relevant to physical health, indicating a poorer HRQoL.	on difficult or unclear terms which were changed before testing.	with children and comments from experts in the field.			t Self-report $\alpha = 0.91$. Proxy report α=0.90.	available for general use.		
PROMIS PGH-7	Single factor analysis showed good fit of child-report and proxy-report items.	Each item was examined for differential item functioning for age, sex, ethnicity and race. No item showed significant differential item	Pilot testing of instrument before final instrument was tested.	Developed from extensive research on PROMIS paediatric item-bank. Item-scale	Internal Consistency 0.84.		Test-retest 0.74.	Proxy-completion 1-2 minutes. Cost: Free		[151]

	The items were also equivalent between age groups for both child and proxy samples.	functioning.		correlation from 0.30 to 0.71.						
TEDQoL	Comparison to PedsQL: moderate positive correlation. Significant positive correlation between ability and happiness rating. Furthermore, there was a significant positive correlation between ability on the TEDQoL and PedsQL score and between happiness and the PedsQL score. No significant		Testing of phrasing of questions during the development procedure.	Item generation was guided by review of literature and previous work with children. Changes were made during testing of the original instrument TEDQoL 1 before TEDQoL 2 was accepted.	Internal Reliability for parent form α=0.60 and children form α=0.60			Interview Administered Cost: Free	-	[216]

	correlation between parent-rated TEDQoL scores and parent-rated PedsQL score.									
FS II(R)	Highly significant correlation between number of days in hospital/absent from school and children with ongoing medical problems.	**Convergent Validity** Children without medical problems score higher than healthy children. **Discriminant Validity** Children who look different from healthy children or children who cannot engage in the same level of physical activity as healthy children or children with poorer cognitive levels all have lower overall scores compared to healthy children. There is more variation in scoring amongst ill children than healthy children.	The form was reviewed by a panel of experts. The FS II(R) was developed from the feedback gathered from the FS I	The FS I was reviewed by a panel of experts to review content validity.	The Internal consistency is $\alpha \geq 0.84$ for all dimensions.			Cost: $25	Summary score	[44] [45]

EQ-5D-Y proxy	Agreement between self-report EQ-5D-Y and EQ-5D-Y proxy version 72.9 – 97.1%	**Convergent Validity** Reported as being similar to validity observed with the EQ-5D-Y (moderate-high). No values or comparison measures/groups were specified in abstracts. **Discriminant Validity** Known group validity was an aim under methodology but not reported under results in the abstract.	Cognitive interviews with the target population to investigate comprehensibility and acceptance.	Developed from a well-accepted and validated adult measure.			Test-retest showed >88% agreement	Excellent comprehensibility. Perceived difficulty <2 in all dimensions except mobility where the value was higher. Cost: Free	Consideration for preference based	[222] [40]

10.2 Appendix 2 Ethical Approval

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences

Human Research Ethics Committee

Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492 • **Facsimile** [021] 406 6411
Email: Sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/research/humanethics/forms

22 May 2014

HREC/REF: 336/2014

Prof J Jelsma
Department of Physiotherapy
Health & Rehab Sciences
F-45
OMB

Dear Prof Jelsma

Project Title: DEVELOPMENT OF AN ENGLISH HEALTH RELATED QUALITY OF LIFE (HRQoL) INSTRUMENT FOR CHILDREN UNDER SIX YEARS OF AGE, DERIVED FROM THE EQ-5D-Y, TO BE COMPLETED BY PROXY-MSc-J Verstraete

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

It is a pleasure to inform you that the HREC has **formally approved** the above mentioned study.

Approval is granted for one year until the 30 May 2015.

Please submit a progress form, using the standardised Annual Report Form, if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

We acknowledge that the following student:- J Verstraete is also involved in this project.

Please note that the on-going ethical conduct of the study remains the responsibility of the principal investigator

Please quote the HREC REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

Hrec/ref:336/2014

Federal Wide Assurance Number: FWA00001637.

Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Hrec/ref:336/2014

10.3 Appendix 3 Institutional Approval

DR T A BLAKE
MANAGER MEDICAL SERVICES
thomas.blake@westerncape.gov.za
0216585788/0828225553
12 JUNE 2014

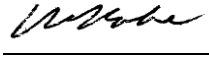
MS JANINE VERSTRAETE
PHYSIOTHERAPY DEPT
RCWMCH

Dear Ms Verstraete,

RESEARCH: DEVELOPMENT OF AN ENGLISH HEALTH-RELATED QUALITY OF LIFE INSTRUMENT FOR CHILDREN < SIX YEARS OF AGE

Approval is hereby granted to commence the research.

Yours faithfully



12 JUNE 2014

DR TA BLAKE **DATE**

CHAIRPERSON

HOSPITAL RESEARCH REVIEW COMMITTEE

10.4 Appendix 4 EQ-5D-Y Proxy

Health Questionnaire

English version for the UK

Script for proxy version of the EQ-5D-Y: 1

(The purpose of this questionnaire is to explore how a care-giver or someone who knows the child well (proxy), would rate the health status of the child. The proxy should not answer on behalf of the child, but rather rate the child's health status as the proxy sees it)

EQ-5D-Y

Describing the child's health today

Under each heading, mark the ONE box that best describes how **you** would describe the health state of the child TODAY.

Mobility(walking about)

He/she has no problems in walking about ❑

He/she has some problems walking about ❑

He/she has a lot of problems walking about ❑

Looking after myself

He/she has no problems washing or dressing him/herself ❑

He/she has some problems washing or dressing him/herself ❑

He/she has a lot of problems washing or dressing him/herself ❑

Doing usual activities (for example: going to school, hobbies, sports, playing, doing things with family or friends)

He/she has no problems doing his/her usual activities ❑

He/she has some problems doing his/her usual activities ❑

He/she has a lot of problems doing his/her usual activities ❑

Having pain or discomfort

He/she has no pain or discomfort ❑

He/she has some pain or discomfort ❑

He/she has a lot of pain or discomfort ❑

Feeling worried, sad or unhappy

He/she is not worried, sad or unhappy ❑

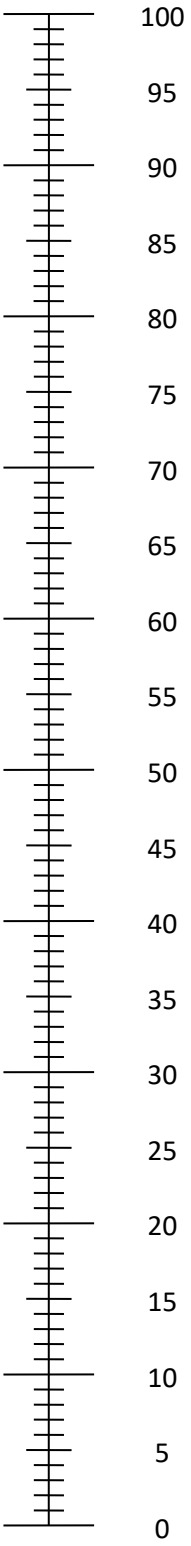
He/she is a bit worried, sad or unhappy ❑

He/she is very worried, sad or unhappy ❑

How good is the health of the child TODAY

- We would like to know how good or bad you think the child's health is TODAY.
- This line is numbered 0 to 100.
- 100 means the <u>best</u> health you can imagine.
  0 means the <u>worst</u> health you can imagine.
- Please, mark an X on the line that shows how good or bad you think the child's health is TODAY.

The best health that you can imagine



The worst health that you can imagine

10.5 Appendix 5 Cognitive Interviews with Caregivers

Cognitive interview with caregiver about EQ-5D-Y Proxy

Child's Name: _____ Date:_____

Institution: Acute Care Chronic Care Day-care centre

Date of Birth of Child: _____

Sex of Child: Male Female

Relationship of Caregiver to child: Mother Father Grandmother

Aunt Uncle Grandfather

Other: _____

Medical Condition of Child as Diagnosed by Doctor: _____

Medication: _____

Medical Care: _____

Mobility Dimension:

1) Why did you answer the question in that way?

   _____

2) What behaviour did the child show that let you to that decision?

   _____

3) Did you compare your child to other children of the same age or to how your child normally behaves? Why?

   _____

4) Do you think this is a relevant question to help us understand the Health-Related Quality of Life of your child? Why?

_____

5) Was the question clear? If no, what was not clear?

_____

6) Were the responses clear? If no, what was not clear?

_____

7) How would you change the question to be more suitable for your child and their age?

_____

Self-Care Dimension:

8) Why did you answer the question in that way?

_____

9) What behaviour did the child show that let you to that decision?

_____

10) Did you compare your child to other children of the same age or to how your child normally behaves? Why?

_____

11) Do you think this is a relevant question to help us understand the Health-Related Quality of Life of your child? Why?

_____

12) Was the question clear? If no, what was not clear?

_____

13) Were the responses clear? If no, what was not clear?

_____

14) How would you change the question to be more suitable for your child and their age?

_____

Usual Activities Dimension:

15) Why did you answer the question in that way?

_____

16) What behaviour did the child show that let you to that decision?

_____

17) Did you compare your child to other children of the same age or to how your child normally behaves? Why?

_____Do you think this is a relevant question to help us understand the Health-Related Quality of Life of your child? Why?

_____

Was the question clear? If no, what was not clear?

_____Were the responses clear? If no, what was not clear?

_____

18) How would you change the question to be more suitable for your child and their age?

_____

Pain/Discomfort Dimension:

19) Why did you answer the question in that way?

_____W

hat behaviour did the child show that let you to that decision?

_____

20) Did you compare your child to other children of the same age or to how your child normally behaves? Why?

_____

21) Do you think this is a relevant question to help us understand the Health-Related Quality of Life of your child? Why?

_____W

as the question clear? If no, what was not clear?

_____

22) Were the responses clear? If no, what was not clear?

_____

23) How would you change the question to be more suitable for your child and their age?

_____

Emotional Dimension:

24) Why did you answer the question in that way?

_____W

hat behaviour did the child show that let you to that decision?

_____

25) Did you compare your child to other children of the same age or to how your child normally behaves? Why?

_____

26) Do you think this is a relevant question to help us understand the Health-Related Quality of Life of your child? Why?

_____W

as the question clear? If no, what was not clear?

_____

27) Were the responses clear? If no, what was not clear?

_____

28) How would you change the question to be more suitable for your child and their age?

_____

Rating of Health:

29) Why did you answer the question in that way?

_____

30) What behaviour did the child show that let you to that decision?

_____

31) Did you compare your child to other children of the same age or to how your child normally behaves? Why?

_____

32) Was the question clear? If no, what was not clear?

_____

33) Would you change the layout or the wording to make it easier to understand? If yes, how would you change it?

_____

General:

34) Do you think any items need to be added to the questionnaire? If so what?

_____

35) Do you think any items need to be taken out of the questionnaire? If so what?

_____

36) Did you think the questionnaire was easy to fill in? If no, why?

Would you change the layout of the questionnaire to make it easier to understand? If yes, how?

Would you change the headings? If yes, how?

_____

37) Would you change the layout of the headings? If yes, how?

_____

38) Any other comment which you feel could help improve this questionnaire?

_____

Thank you.

10.6 Appendix 6 Informed Consent for Cognitive Interviews

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences

School of Health and Rehabilitation Sciences

Division of Physiotherapy
F45 Old Main Building, Groote Schuur Hospital,
Observatory 7925
Tel: +27 (0) 21 406 62505
Fax: +27 (0) 21 406 6323

Informed consent from caregivers taking part in the study

Information Sheet

Title of the Study: Development of an English Health-Related Quality of Life measure for children under seven years of age, derived from the EQ-5D-Y, to be completed by proxy.

Dear Parents,

I am doing a research project as part of my Master's degree in physiotherapy. I want to look at how you answer a questionnaire about your child's Health-Related Quality of Life. I want to ask you a few questions about your child. After that I will ask you about why you answered the questions the way that you did.

I want to know what you were thinking when you answered the questions. I want to find the most important questions to ask about a child's quality of life. I also want to know if I need to ask different questions for different aged children. Or if I must explain what children should be doing at different ages. The information that I get will help me to develop a questionnaire that will be better for young children.

I will ask you to fill-in a few questions about your child's quality of life. The questions will be about how your child moves, help with looking after them self, how they spend their free time and if they have pain or feel worried. I will then ask you a few questions about the form so that I can understand how you answered the questions. This should not take longer than 20 minutes. All the other caregivers of children under six are being invited to take part at this facility and others.

It is your choice to take part in this study and you do not have to agree if you don't want to. If you choose not to take part in the study, nothing bad will happen to you or your child. If you agree now but decide later that you don't want to do it anymore, you can let us know and all of the information that you have given us will be taken out of the study. We will be grateful if you would help us by agreeing to let us interview you. If you decide to be part of the study, the treatment and care that your child is getting will not be changed in any way and will carry on as normal.

Your child's name will be written on the form. If we find anything that worries us we can let you know. We will talk to you about the problem and if you agree we can ask a doctor or a therapist to assess your child. All the information that you give will be confidential. Your child's name will be deleted when we study the information. If we publish what we find, nobody will know that you took part or what you answered. The

information will be collected by myself and stored onto a secure computer with a password. The information that you give will only be used for this study.

There are no risks in taking part in this study. You will not be given any money for being part of the study. I will be comparing the information that you give me to caregivers of other children who are sick. I hope that this will help us to understand the quality of life of children better and to improve the way we look after all children in the future.

If you have any questions or concerns about the study you may contact the researcher or the supervisor:

Researcher	Supervisor
Janine Verstraete	Professor J. Jelsma
Red Cross War Memorial Children's Hospital	University of Cape Town
Division of Physiotherapy	Department of Health &Rehabilitation Sciences
S13 Out Patients Building	Division of physiotherapy
Klipfontein Road	F45 Old Main Building
Rondebosch	Groote Schuur Hospital
Tel: 021 658 5033	Observatory
Cell: 082 840 9293	Tel: 021-406 6401

If you have any questions about your rights or welfare as a research participant please contact:

Professor M. Blockman

The University of Cape Town

Faculty of Health Sciences Human Research Ethics Committee

Tel: 021 406 6492

Room: E52.24 Old Main Building

Consent Form

Please can you read through the table below and mark off your answer with an X

Declaration	Yes	No
I have read through the information provided and understand it.		
I understand that my consent is required.		
I understand that it is my choice to take part and I can refuse my consent without any consequences to myself or my child.		
I understand that not agreeing to take part in the study will not change the way they are treating my child now or in the future.		
I understand that nobody will know that either my child or I took part in the study if it is published.		
I consent to taking part in this research of my own free will.		

Signed:

Caregivers signature

Date

Researcher signature

Date

10.7 Appendix 7 Descriptive Tables per Dimensions and Age Group from the Cognitive Interviews

10.7.1 Mobility Dimension

Table 10-3 Description of Answers for Mob Dimension for Children Aged 0-1 years

0-1 year	**AI**	**CI**	**TD**
Mob :3* (10)	4	4	2
Reason for answer	Age – too young (4) Illness will not allow child to walk in the future (1)	All developmental milestones are delayed (3) Age – too young (1)	Age – too young (2)
Observable behaviour	See that he is unable to walk (4) Does not expect child to walk due to illness (MMC) (1)	See that he is unable to walk (2) Child has not yet achieved milestones appropriate for age such as sitting (2)	Due to young age it is not expected (2)
Mob : 2* (0)	0	0	0
Mob : 1* (2)	0	0	2
Reason for answer			Crawling and attempts to stand (1) Able to walk (1)
Observable behaviour			Crawling, standing, cruising (1) Walking (1)
Alternate items	General movement (3) Kicking (2) Upper limb movement (2) Communication (1) Senses – seeing, hearing (1) Socialize (1)	General movement (2) Play (2)	Walking as opposed to walking about (1) Communication (1) Socialize (1) Upper limb movement (1) Movement (1)

Comparison: Normal Behaviour (7)	3	3	1
Reasons	Age – too young (2) Unique and will develop differently due to illness (1)	Cognisant of developmental milestones (1) Monitor improvement (2) Acceptance of chronic condition but cognisant of normal development (1)	Each child is different and development between them will differ (1)
Comparison: Other Children (5)	1	1	3
Reasons	Hope to return to pre-Morbid function (1)		Guide for development (2)
Importance for HRQoL: Yes (7)	1	3	3
Reasons	A hospitalised child can't run around and be themselves (1)	Movement is important (1) Too young to walk but frustrated at not being able to move (1) Important for child (1) Important for ability to go to school (1) Child has a desire to walk (1)	If he were unhealthy it would affect ability to move (1) Every child deserves to walk (1) Burden of care increases if a child can't walk (1) It is a requirement to walk (1)
Importance for HRQoL: NO (5)	3	1	1
Reasons	Inappropriate – children under 1 year are not yet walking (3)	Age – no impact on not being able to walk now but as he gets older it will become important (1)	Ability to move is more important for a child younger than 1 year than walking (1)

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-4 Description of Answers for Mob Dimension for Children Aged 1-2 years

1-2 years	**AI**	**CI**	**TD**
Mob :3* (4)	2	2	0
Reason for answer	Not yet walking (2) Unable to sit (1)	Can't walk at all (1) Trying to walk with furniture (1)	
Observable behaviour	Attempting to hold onto furniture (1) Unable to walk (1)	Unable to walk (1) Attempting to walk (1)	
Mob :2* (1)	1	0	0
Reason for answer	Learning to walk again (1)		
Observable behaviour	Wobbly with walking (1)		
Mob : 1* (7)	1	2	4
Reason for answer	Walking well (1)	Walking well (2) Running (1)	Walking well (4)
Observable behaviour	Walking well holding onto cot (1)	Walking as other children (2) Running (1)	Walking well (3) Moves around without difficulty (1) Running (1) Active (1) Independent (1)
Alternate items	Include all movement; not just walking (1)		
Comparison: Normal Behaviour (6)	2	4	0
Reasons	Walking well (1) Pre-morbid function was normal (1)	More intelligent than others (1) God's will (1) Will achieve it when he is ready (1) More advanced than others (1)	

		Individual (1) Applaud his improvement (1)	
Comparison: Other Children (6)	2	0	4
Reasons	Guide for development – younger children are able to walk (1) Hope that child can learn to walk like others (1)		Guide for development (4) Compare to developmental milestones (1)
Importance for HRQoL: Yes (11)	3	4	4
Reasons	Something wrong if you don't walk by this age (2) Need to help a child who can't walk. Need to teach him and find a cure (1)	Unsure (1) Burden of Care (1) If there was a problem someone can identify it and rectify it (1) It would be a problem in the future more than now as he is still small (1)	Inability to move limits life exposure (1) Frustrated at not being able to move (1) Important for exploring and learning (1) If not walking need to seek help (1) She will standout if she is different (1)
Importance for HRQoL: NO (1).	1	0	0
Reasons	Unknown (1)		

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-5 Description of Answers for Mob Dimension for Children Aged 2-3 years

2-3 years	**AI**	**CI**	**TD**
Mob :3* (4)	1	3	0
Reason for answer	Unable to walk (1)	Unable to walk (1) Not walking, but crawling (1) Paralysed and can't walk (1)	
Observable behaviour	Previously walking but not anymore (1)	Unable to walk (1) Crawling (1)	
Mob :2* (0)	0	0	0
Mob : 1* (8)	3	1	4
Reason for answer	Walking (2) Running (1) Speaking and doing everything (1)	Walking (1)	Walking (4)
Observable behaviour	Walking (2) Running (1)	Stable and walking well (1)	Walking well (3) Running (1) Normal activities like others (1) Moves quickly and easily (1) No limiting physical disability (1)
Alternate items		Having fun (1) Playing (1)	
Comparison: Normal Behaviour (4)	1	2	1
Reasons	Unknown (1)	Acceptance of child's condition (1) Pre-morbidly normal – to gauge recovery (1)	He is well; no need to compare (1)
Comparison: Other Children (8)	3	2	3

Reasons	Previously well hopeful that function will return (1) Walking like others (1) Developmentally on par (1)	Children should do the same thing at the same age (1) Other children her age can walk and she can't (1)	I compare to see how she is doing because she was premature (1) Ensure no problems (2) See what children of the same age are capable of (1)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Frustration if unable to walk (1) Child wants to walk (1) Child wants to play (1) The child worries when he is unable to walk (1) Assess if she is well (1) I don't know how it would be (1)	Important to know how she is moving (1) Determine ability (1) Find solutions or help (2) Understand why they can't walk (1) Affects parent more than the child (1) He can still learn to walk (1)	Independence for tasks and eating (2) Involved and active (1) Frustrated (1) Busy – doesn't like to still (1)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-6 Description of Answers for Mob Dimension for Children Aged 3-4 years

3-4 years	**AI**	**CI**	**TD**
Mob :3* (3)	1	2	0
Reason for answer	Not yet walking (1)	Unable to walk (2)	
Observable behaviour	Not walking (1)	Physio is teaching her how to walk (1) Bum shuffles but can't walk (1)	
Mob :2* (0)	0	0	0
Mob : 1* (9)	3	2	4
Reason for answer	Walking (3)	Walks well (2) Determined and doesn't struggle (1)	Walking well (4) Competent with all activities and gross motor function (1)
Observable behaviour	Walking well (1) Walks but tires (1) Walks when he has to (1)	Walks well (1) Running and jumping (1)	Walking well (4)
Alternate items	Quantify quality of walking, distance and tiredness (1) Walking instead of walking about (1)	Independent Mobility (1)	
Comparison: Normal Behaviour (5)	2	3	0
Reasons	She is normal (1) Concerned about pain and that she wouldn't move like before (1)	Individual (2) Determined (1) Slower than other children (1) Monitor progress (1)	
Comparison: Other Children (7)	2	1	4
Reasons	Tires easily compared to others (1)	Good indication of what his abilities	He is better than others (1)

	Other children her age are walking (1)	should be (1)	Same abilities as others (3)
Importance for HRQoL: Yes (10)	4	2	4
Reasons	Asses what is wrong (1) It affects the parent more than the child (1) Provide help (1) Hurtful to see others walking and playing if he is unable (1)	Not always able to achieve everything with illness (1) Mobility gives an indication of health e.g. Brain and spine (1)	Mobility affects function (1) Emotional – he would be sad (1) Seek help (1) Emotional for parent (1) Want to do what others are doing (1)
Importance for HRQoL: NO (2)	0	2	0
Reasons		She will be happy if she walks or not (1) It doesn't bother her now – maybe later in life (1)	

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-7 Description of Answers for Mob Dimension for Children Aged 4-5 years

4-5 years	**AI**	**CI**	**TD**
Mob :3* (1)	0	1	0
Reason for answer		Unable (1)	
Observable behaviour		Wheelchair bound (1)	
Mob :2* (4)	2	1	1
Reason for answer	Abnormal gait due to injured foot (1) Poor leg development from rickets (1) Restricted by drip and hospital cot (1)	Poor balance (1)	Worried and feeling unwell with standing (1) Pain (1) Not asking to walk (1)
Observable behaviour	Poor balance (1) Abnormal gait pattern (1)	Difficulty with balance especially on uneven ground (1)	Facial expression shows that she does not want to walk (1)
Mob : 1* (7)	2	2	3
Reason for answer	Walking well (2)	Not complaining (1) Free, to do what he wants (1)	Walks into walls when distracted – but that is a concentration problem (1) More advanced than others(1) Climbs and is very active (1) Normal (1)
Observable behaviour	Walking and running (2)	Walking well (2)	Walking (3)
Alternate items	Walking instead of walking about (1)		
Comparison: Normal Behaviour (4)	2	1	2
Reasons	Pre-morbid function was normal (1) Unique; not fair to	All children are different (1)	Limited exposure to other children (1) Not normally worried

	compare (1) Her accomplishments bring us joy (1)		and walked well (1)
Comparison: Other Children (7)	2	3	2
Reasons	Not the same as others due to weakness and poor speech (1) Same as other children (1)	Question how things would be without disability (1) Guide- to see that she walks normally (1) Measure extent of improvement (1)	Doing well for her age (1) Obvious that he is fine when compared to other children (1)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	To help the child (1) Unable to play with friends (2) Frustrated (2) Wants to walk (1)	Better view of life if you are not dependent for mobility (1) Frustrated (1) Delayed walking due to illness but he was determined to do the same as others (1) Unable to play Independently if she can't walk because she gets hurt (1) Limiting if unable to move around with peers (1)	Learn independence (2) Unable to run with friends and participate in sport (1) Emotional – feel inferior (1) Limit ability to learn through play and exploration (1) Monitor development (1) Identify potential problems (1)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-8 Description of Answers for Mob Dimension for Children aged 5-6 years

5-6 years	**AI**	**CI**	**TD**
Mob :3* (2)	2	0	0
Reason for answer	Not walking (2) Awaiting wheelchair (1) Since the accident she will never walk again (1)		
Observable behaviour	Not walking (2) Crawling (1)		
Mob :2* (4)	2	1	1
Reason for answer	Struggles to walk (2)	Walking but falling to the side (1)	She burnt her leg last week and it is sore (1)
Observable behaviour	Tires and shakes with long distances (1) Walking on toes (1) Falling (1)	No balance (1) Falling (1) Flapping hands (1)	Limping (1)
Mob : 1* (6)	0	3	3
Reason for answer		Walking well (3) Very active (1)	Walking well (1) Energetic (1) Not paralysed or limping (1)
Observable behaviour		Walking (1) Tires with running (1)	Runs (1) Walks well (1)
Alternate items	Movement for function (1) Crawling (1) Play (1) School (1)		
Comparison: Normal Behaviour (7)	2	3	2
Reasons	Can't play with children her age as	Other children his age are walking well and	She is fine (1) Walking well before

	she is slower and gets tired (1) I accept her condition (1)	he is not (1) Unique/ Individual (1) No concerns (1)	the burn (1)
Comparison: Other Children (5)	2	1	2
Reasons	If she could walk like others she would be perfect (1) He doesn't walk like other children (1)	Plays and walks well (1)	Walks like others (2)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Unable to play (3) Affects interaction with peers (1) Parent worry about gait (1)	Inform health care professionals (1) Illnesses like asthma affect mobility (1) Seek help (1) Important for parent (1) Child gets joy from walking, dance, sport and socialising with peers (1) So many other functions come from being able to walk (1)	Gauge wellness of child (2) Schooling (1) Burden of care (1) Independence (1) Toileting (1) Stressed about not walking well (1) Desire to walk well (1)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-9 Description of Answers for Mob Dimension for Children Aged 6-7 years

6-7 years	**AI**	**CI**	**TD**
Mob :3* (0)	0	0	0
Mob :2*(2)	1	0	1
Reason for answer	Likes to walk around but is limited due to risk of infection (1)		He is clumsy with spatial relation problems (1)
Observable behaviour	Limited to where she can walk (1)		Bumps objects, hurts himself and stubs his foot (1)
Mob : 1* (10)	3	4	3
Reason for answer	Running as soon as the drip comes off (1) Loves walking (1) Playing and walking well (1)	Walks well (2) Runs (2) Runs, walks and finds his way back (1)	Walking well (3)
Observable behaviour	Running (1) Walking (2) Playing (1)	Walks well (4) Runs (3)	Walking well (3) Runs and Jumps (1)
Alternate items	No	No	No
Comparison: Normal Behaviour (10)	4	3	3
Reasons	Unknown (1) Unique (1) Monitor medical recovery (1) Improvement as previously confined to bed (1) Knowledge of own child (1)	I don't treat or look at him differently (1). Previously sick and couldn't walk until 2 years. Now I am satisfied (1). Limited interaction with other children (1).	No problems otherwise I would compare to others (1) No problem (1) I thought boys were clumsy so I never looked at other children until I was told to (1)
Comparison: Other Children (2)	0	1	1
Reasons		Due to condition I use	Recognise

		others as a guide (1)	abnormalities early (1)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Inability to walk implies illness (1) Independence (1) With surgery my daughter was unable to walk and was very frustrated and withdrawn(1) Unknown(1) Tires with walking and can't always play with friend or walk to the shop like others (1)	Reduced QoL (1) Parent worry about the child's self-image (1) Independence (1) Mobility is important for play (2) Child will get frustrated and moody (1) Lack of mobility affects emotions (1)	Emotional (2) Seek help if it is identified (2) Independence (1)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

10.7.2 Self-Care Dimension

Table 10-10 Description of Answers for SC Dimension for Children Aged 0-1 years

0-1 years	**AI**	**CI**	**TD**
SC :3* (10)	4	2	4
Reason for answer	Too young (4)	Too young (2)	Too young (4)
Observable behaviour	Caregiver washes and dresses child (4)	Too young (2)	Too young (4)
SC :2* (0)	0	0	0
SC level : 1* (2)	0	2	0
Reason for answer		He likes to be washed and dressed (1) I wash and dress him every day (1)	
Observable behaviour		Child is washed and dressed (1)	
Alternate items	Eating (4) Sleeping (2) Communication (1)	Eating (2) Sleeping (2) Communication (2)	Eating (2) Communication (4) Sleeping (2) Play (1) Senses (1)
Comparison: Normal Behaviour (8)	4	2	2
Reasons	Too young to wash and dress (4)	Accepted my child's condition and will never compare her (1) He is my child (1)	She is still young (1) All children learn at different paces (1)
Comparison: Other Children (4)	0	2	2
Reasons		Other children under one cannot wash or dress (2)	Others also need to be washed and dressed at this age (1)
Importance for HRQoL: Yes (5)	4	0	1

Reasons	Unknown (1) He looks after himself in other ways (1) Looks after himself with eating (2) and sleeping (1)		SC is important, but it is different for each age group. At this age he is able to cry for us to help with his care (1)
Importance for HRQoL: NO (7)	0	4	3
Reasons		No children of this age can wash or dress (4)	Not important in this age group (3)

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-11 Description of Answers for SC Dimension for Children Aged 1-2 years

1-2 years	**AI**	**CI**	**TD**
SC :3* (11)	4	3	4
Reason for answer	Too young (4)	Too young (3)	Too young (4)
Observable behaviour	Mother washes and dresses child (4)	Mother washes and dresses child (3)	Mother washes and dresses child (4)
SC :2* (1)	0	1	0
Reason for answer		He is only one (1)	
Observable behaviour		Mother washes and dresses child (1)	
SC* level : 1	0	0	0
Alternate items	Play (2) Eating (4) Sleep (1) Potty training (1)	Eating (2) Communication (2)	Communication (4) Eating (2) Sleep (1) Potty training (2)
Comparison: Normal Behaviour (4)	1	2	1
Reasons	Every child develops differently (1)	She only helps (1) She is not like others (1)	She is fine; not expected to do these tasks (1)
Comparison: Other Children (8)	3	2	3
Reasons	Other children of this age are not washing or dressing either (4)	Other children of this age are not washing or dressing either (2)	Other children of this age are not washing or dressing either (3)
Importance for HRQoL: Yes (3)	2	1	0
Reasons	He looks after himself in other ways (1) He needs help with a lot of things (1)	We need to know how she is (1)	
Importance for HRQoL: NO (8)	2	2	4

Reasons	Not age appropriate (2)	Not age appropriate (2)	Not age appropriate (4)

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-12 Description of Answers for SC Dimension for Children Aged 2-3 years

2-3 years	**AI**	**CI**	**TD**
SC :3* (7)	4	3	0
Reason for answer	Unable to wash or dress –too young (3) He doesn't want to wake up and wash (1) He doesn't want to be washed in hospital (1) Normally he likes the water and helps to wash (1) Should start helping with washing and dressing (1)	Not yet learned the skill (1) Can't dress herself (1) Unable to wash or dress (1)	
Observable behaviour	Unable to wash and dress independently (1) Doesn't want to be washed or dressed (2) Not assisting with washing and dressing (1)	Trying but not succeeding (1) Assisting but unable to do it independently (2)	
SC :2* (3)	0	0	3
Reason for answer			Age appropriate problems – needing help with fastenings and tight tops, not thorough and consistent with washing (1)

			Still young and needs help (1) Doesn't want to get dressed but when he does there is no problem (1)
Observable behaviour			Assistance with fastenings (1) Not thorough with washing (1) Needs help (1) Resistant (1)
SC level : 1* (2)	0	1	1
Reason for answer		She is potty trained, washes and dresses herself (1)	She is young so I do it for her (1)
Observable behaviour		Able to wash and dress (1)	Chooses own clothes (1)
Alternate items	Sleeping (1) Eating (2) Communication (2) Potty training (1)	Potty training (1) Eating (1)	Motivation and interest in SC (1) Sleeping (1) Eating (2) Potty training (2) Communication (1)
Comparison: Normal Behaviour (6)	1	2	3
Reasons	Normally a happy child who loves to bath (1)	She is learning (1) If I compare to other children I will be constantly worried. If I compare him to himself I can monitor his improvement (1)	She is fine (1) I don't see other children while they are washing and dressing (1) I didn't think of comparing (1)
Comparison:	3	2	1

Other Children (6)			
Reasons	If he could see he would copy other children (1) Should be able to do what others do (1) Other children can't wash or dress (1)	Other children can do more than her (1) She is better with washing and dressing; she is clever and good with learning (1)	Other children can't wash or dress (1)
Importance for HRQoL: Yes (10)	3	4	3
Reasons	Start to look after themselves - independence (1) Looking after herself is important; not necessarily washing and dressing (1) Important for his caregivers (1)	Seek help if there is a problem (1) Reliant on caregiver with tasks others can do and can therefore not go to school (1) Develop independence (1) Help improve areas that are lacking (1) Not a problem now but will affect him when he is older (1)	We must know if she can manage – but it won't affect her now because she is young (1) It is important for learning (1) Important for independence (1)
Importance for HRQoL: NO (2)	1	0	1
Reasons	He is young so it is fine to be washed and dressed (1)		I don't think it is important to him or that it will impact him at this age (1)

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-13 Description of Answers for SC Dimension for Children Aged 3-4 years

3-4 years	**AI**	**CI**	**TD**
SC :3* (5)	3	0	2
Reason for answer	Assisting with washing and dressing (2) Dependent for washing & dressing (2)		I need to wash and dress him. He helps(1) Helps sometimes (1)
Observable behaviour	Assisting with SC (2) Totally dependent (1)		Assistance with SC (2)
SC :2* (3)	0	3	2
Reason for answer		No problem with washing; some problem with t-shirt as weak on the left (1) Plays in the bath; starting to dress himself more (1) Not able to put pants on; helps with washing (1)	Difficulty with buttons and belts. Doesn't see washing as important but rather something I do to him (1) Washes and dresses but I must check if it is done properly (1)
Observable behaviour		Needs assistance (3)	Needs assistance(2)
SC level : 1* (2)	1	1	0
Reason for answer	I am washing him today as I do at home (1)	I wash and dress her every day and she doesn't have a problem with it (1)	
Observable behaviour	Being washed (1)	Being washed and dressed (1)	
Alternate items	Assist with washing and dressing (1) Eating (1) Communication (1)	Independence (1) Learning (1) Cognition (1) Communication (1) Eating (1) Potty-training (1)	Assist with washing and dressing (1) Potty training (2) Eating (2)

Comparison: Normal Behaviour	3	2	2
Reasons	Unique (1) I know my child (1) I am the one who hasn't taught him (1)	She is special and I love her (1) She is different and it would not be a fair comparison (1)	All children need help; but he does try (1) More advanced than others (1)
Comparison: Other Children	1	2	2
Reasons	Others her age can't do it either (1)	Others also struggle at this age (1) All children develop slightly differently (1)	Comparison to my other children (2)
Importance for HRQoL: Yes (9)	3	2	4
Reasons	If she couldn't she would always be reliant on us – it would worry us as parents (1) It's part of life (1) She must learn (1)	Part of developmental process (1) I wish she could help with washing and dressing (1)	Assisting indicates development of cognition and fine motor skills(1) independence (2) Follow routine and rules (1)
Importance for HRQoL: NO (3)	1	2	0
Reasons	It is normal to still have help with washing and dressing (1)	It doesn't hamper child's QoL not to wash and dress – maybe their independence (1) Others of this age can't wash and dress either (1)	

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-14 Description of Answers for SC Dimension for Children Aged 4-5 years

4-5 years	**AI**	**CI**	**TD**
SC :3* (3)	2	1	0
Reason for answer	Unable due to weakness (2)	Dependent on me for everything and feeding (1)	
Observable behaviour	Unable to wash or dress (2)	Dependent for all care (1)	
SC :2* (2)	0	0	2
Reason for answer			Supervision with dressing and helps with washing (1) She is stubborn and has stopped washing and dressing as she wants attention with a new sibling (1)
Observable behaviour			Needs supervision (1) Stopped washing and dressing (1)
SC level : 1* (7)	2	3	2
Reason for answer	Needs help to wash; dresses Independently (2)	Wants to do it himself (1) Does everything herself (1)	Wash and dress independently (2)
Observable behaviour	Needs help with washing (1) Struggles with zips, buttons and laces (1)	Washes himself in the bath we just watch (1) Struggles with zips, buttons and laces (1) Struggles with the taps otherwise she can do it all (1)	Wash and dress independently (2)
Alternate items	Independence (2) Eating (1)	Eating (2) Communication (1)	Following rules (1) Potty training (2)

		Potty training (1)	Eating (2) Communication (1)
Comparison: Normal Behaviour (10)	3	3	4
Reasons	Previously able to wash and dress independently (1) I am just interested in him (1) We compare *her* one day to the next (1)	Monitor improvement (1) He is going through a difficult time which others are not (1) I think we look at our child but mothers talk which gives you a yardstick (1)	Not necessary to compare as he is doing well (1) Limited exposure to children (2) I know how he is (1)
Comparison: Other Children (2)	1	1	0
Reasons	I compare her to her siblings and other children to see how she is doing (1)	Assess if she is on par or needs help (1)	
Importance for HRQoL: Yes (11)	3	4	4
Reasons	Could previously do everything (1) He likes to be independent (1) She is independent and wants to learn (1)	Not important now; independence is important later (1) Independence (2) Important for self-image (1)	Hygiene and personal care are important for social relations (1) Shows learning (1) Independence (3)
Importance for HRQoL: NO (1)	1	0	0
Reasons	Still a baby so it is not important now (1)		

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-15 Description of Answers for SC Dimension for Children Aged 5-6 years

5-6 years	**AI**	**CI**	**TD**
SC :3* (4)	3	1	0
Reason for answer	Unable to wash or dress (2)	I wash and dress him (1)	
Observable behaviour	Requires help – struggling to take socks off (1) Unable to wash or dress (1)	Tries but can only take off his pants and napkin (1)	
SC :2* (2)	0	1	1
Reason for answer		Too young to wash and dress herself (1)	Needs help with pants because she burnt her leg – she could do it on her own before (1)
Observable behaviour		Helps where able (1)	Needs help (1)
SC level : 1* (6)	1	2	3
Reason for answer	Washing and dressing well (1)	Competent and Independent (2)	Wants to do it herself (2) Supervise washing (3) Washes and dresses Independently (1)
Observable behaviour	Washing and dressing well (1)	Washes and dresses Independently (2)	Washes and dresses independently (3)
Alternate items	Potty training (1) Eating (1)	Eating (2) Potty training (1) Dressing only (1)	Potty training (1) Eating (1)
Comparison: Normal Behaviour (8)	3	3	2
Reasons	Independent (1) Dependent on me now more than at home (1) Monitor improvement	Child is unique (1) Age – too young (1) No concern; consider developmental milestones (1)	Limited exposure to other children (1) Before she burnt her leg she was fine (1)

	(1)		
Comparison: Other Children (4)	1	1	2
Reasons	Born normal but because of what happened she is no longer like others (1)	I compare to other children but younger children (1)	I compare dressing because he struggles with buttons and laces (1) She is looking after herself like others (1)
Importance for HRQoL: Yes (10)	4	2	4
Reasons	Monitor development (2) Good to learn to do it themselves (1) She gets upset when she sees others doing what she is unable to do (1)	Monitor development (1) Independence (1)	Important function (1) Independence (3) She is complaining now not being able to do it herself (1)
Importance for HRQoL: NO (2)	0	2	0
Reasons		Too young to impact HRQoL (1) Parents still help a lot at this age; walking is much more important (1)	

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-16 Description of Answers for SC Dimension for Children Aged 6-7 years

6-7 years	**AI**	**CI**	**TD**
SC :3* (1)	0	0	1
Reason for answer			Problems with dressing more than washing. Poor attitude toward SC (1)
Observable behaviour			He is unable to do buttons, zips, shoe-laces and puts clothes on back to front. He is unable to put on socks or match colours of clothes (1)
SC :2* (2)	1	1	0
Reason for answer	Dad had to help him this morning as he is scared being in hospital and weary of the drip. At home he does everything well (1)	Does not wash properly and struggles with tops and shoe-laces (1)	
Observable behaviour	Needed help to wash and dress (1)	Needs help with washing, shoe-laces and tops (1)	
SC level : 1* (9)	3	3	3
Reason for answer	Needs supervision (1) I always wash her, but she dresses herself (1) Doesn't dress; normal for age (1)	Washes and dresses well (3) Moody and doesn't always do it (1)	Able to wash and dress (3) Needs supervision (1)
Observable behaviour	Needs supervision (1) Is washed but dresses independently (1)	Washes and dresses well (3)	Able to wash and dress (3) Needs supervision (1)

	Able to wash but not dress (1)		
Alternate items	No	No	No
Comparison: Normal Behaviour (8)	4	2	2
Reasons	Does everything at home (1) Limited contact with other children (1) I need to look after her (1) Same as other children (1)	Accept child and his condition (1) Moody and doesn't always do it (1)	Limited interaction with others (2)
Comparison: Other Children (4)	0	2	2
Reasons		Ensure he is on par with others (1) Other children are more independent with SC than him (1)	There is another child the same age at home (1) Some children of this age are not able to wash or dress (1)
Importance for HRQoL: Yes (11)	4	4	3
Reasons	Part of everyday life. He doesn't mind help for a short time but not for long (1) Independence (2) Maybe other children struggle more (1)	Independence (1) At the age that he is aware of his functional ability – he would feel helpless and it would affect him emotionally (1) Seek help early if there is a problem (1) Build self-esteem and pride but it will have	Important for learning and independence (1) Would not want someone else doing the tasks he could previously do (1) His inability to dress independently makes him anxious and he worries about it. He behaves badly to draw

		more impact later in life than at this age (1)	attention to his behaviour rather than what he can't do (1)
Importance for HRQoL: NO (1)	0	0	1
Reasons			How they assist with SC rather than independent (1)

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

10.7.3 Usual Activities Dimension

Table 10-17 Description of Answers for UA Dimension for Children Aged 0-1 years

0-1 years	**AI**	**CI**	**TD**
UA :3* (5)	3	1	1
Reason for answer	He is too young (3)	He can't play, walk or go to school (1)	Age – too young (1)
Observable behaviour	Unable to do any UA described (1) Does play with hands, makes noises, smiling, laughing and social interaction (1) He can play with his hands and a rattle (1)	Unable to play (1)	Too young to engage in these activities (1)
UA :2* (3)	0	2	1
Reason for answer		Responds to play (1) There are some things she can do (1)	Very young (1)
Observable behaviour		Able to play (1) Able to crawl, eat by mouth, but not play with toys or other children (1)	He is able to laugh, smile and play with toys or his hands (1)
UA : 1* (4)	1	1	2
Reason for answer	Not going to school, playing sport or hobbies – he is too young. Plays and does his own thing (1)	Likes to play and be around people (1)	Plays with her sister (1) I play with him and he knows what to do (1)
Observable behaviour	Playing (1)	Likes to play and be around people (1)	Loves to play (1) If I sing he dances; he knows how to play with a car and a ball

			and he never forgets (1)
Alternate items	Socialize (2) Communicate (2) Sleeping (1) Eating (1) Play only (1)	Socializing (2) Play only (3)	Eating (2) Play only (2) Communication (2) Sleep (1)
Comparison: Normal Behaviour (8)	3	3	2
Reasons	He is young (1) Monitor change or if anything is wrong (1) Playing well (1)	Compared to others she has lots of problems. Compared to herself she doesn't have as many problems (1) Don't compare her (1) I know what is good for him (1)	Better than other children (1) I don't compare (1)
Comparison: Other Children (4)	1	1	2
Reasons	Same as other children of the same age (1)	I see other children playing in the street and that's what I want for him (1)	Developmentally appropriate for a new-born (1) Compare to other well children in the community (1)
Importance for HRQoL: Yes (10)	3	3	4
Reasons	Struggling to interact for his age and his health is poor which must affect his QoL (1) Not playing well in hospital (1)	To help if there is a problem (2) Needs family and friends to be happy and for support. A playing child is a	It would be terrible if he would stop doing what he could do (1) Your QoL is very poor if you are unable to play. It's painful to

	You must know what children are supposed to do (1)	happy child (1)	parents – I am not sure how the child feels (1) Important as he learns from playing: it builds his body and muscles and interaction with other children (1) Pick up if there is anything wrong – although it is harder for the parent than the child (1)
Importance for HRQoL: NO (2)	1	1	0
Reasons	When he gets older it will be difficult as he will not walk, but not now (1)	I want it for him more than he wants it for himself. I don't think he understands though (1)	

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-18 Description of Answers for UA Dimension for Children Aged 1-2 years

1-2 years	**AI**	**CI**	**TD**
UA :3* (2)	1	1	0
Reason for answer	Young and can't do all of this, playing is important (1)	She doesn't go to school, have hobbies or play sport (1)	
Observable behaviour	Plays nicely with other children and alone (1)	Likes to play (1)	
UA :2*(3)	2	1	0
Reason for answer	The interest and energy with play is not the same as usual (1) He can't walk or be with his friends but he can play (1)	He is playing cricket with his brother but we adapt if for him and he plays on his knees. He is at school (1)	
Observable behaviour	Not playing as before (1) Able to play (1)	Plays with modifications (1)	
UA : 1* (7)	1	2	4
Reason for answer	She can go to school, but not when she is in the hospital. Playing in the hospital but not the same as home (1)	He is playing on his own and does activities appropriate for his age (1) No problems (1)	Plays and dances (1) Surrounded by family, interacts with them and plays all day (1) Too young for school, loves playing and interacts with family and friends (1) Doing exact activities for age (1)
Observable behaviour	Playing (1)	Playing (2) Plays and gets along with other children (1)	Playing and interacting socially (2) Playing (2)
Alternate items	Play only (4) School (1)	Play only (4) Socializing (2)	Play only (4) Communication (1)

			Socializing (1)
Comparison: Normal Behaviour (4)	1	2	1
Reasons	He used to be more interested (1)	No concerns (1) Unique child (1)	We are happy with his playing (1)
Comparison: Other Children (8)	3	2	3
Reasons	To see if he is doing okay (1) Same as others (1) Different to others (1)	Likes to play like other children (1) More advanced than other children (1)	Ensure normal development (3)
Importance for HRQoL: Yes (11)	3	4	4
Reasons	Need to help if there is a problem (1) Monitor improvement (2)	Identify problems (1) Good impact to be able to play and enjoy life (1) If he is sick he doesn't play well and is unhappy (1) Needs to be with other children and interact at school and with playing (1)	Play is important as they learn how to share, talk and discipline (1) Play helps develop: communication; physical activity; spiritual and emotional wellbeing (1) If he were unhealthy, unable to walk or hurt he would be unable to play affecting his fine motor skills, learning and development (1) Seek help before it develops further (1)
Importance for HRQoL: NO (1)	1	0	0
Reasons	She is playing well (1)		

1* No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension

Table 10-19 Description of Answers for UA Dimension for Children Aged 2-3 years

2-3 years	**AI**	**CI**	**TD**
UA :3* (3)	1	2	0
Reason for answer	Unable to see; not playing as before (1)	Scared and clingy – doesn't easily play with (1) Unable to run or play. Needs specialised schooling (1)	
Observable behaviour	Unable to play with toys (1)	Doesn't easily play with others (1) Unable to play or attend school (1)	
UA :2*(2)	1	1	0
Reason for answer	Unable to keep up with others, unable to attend school or be with family as hospitalised (1)	Playing well but no hobbies, sport or school due to young age (1)	
Observable behaviour	Shortness of breath with running and unable to go to school or see family and friends (1)	Playing well (1)	
UA : 1* (7)	2	1	4
Reason for answer	Playing well (2) Too young to go to school have hobbies or play sport (1)	Always playing with others (1)	Attends school and loves playing with others (3) Anxious going anywhere without mom (1)
Observable behaviour	Playing well (1)	Playing well (1)	Plays with others (3) Self-limited by anxiety (1)

Alternate items	Play only (3) Socializing (2)	Play only (3) Socializing (1)	Play only (3) School (2) Hobbies (1)
Comparison: Normal Behaviour (9)	4	3	2
Reasons	He has lost his eyesight (1) Like this at home (2) Monitor dyspnoea with lung problem (1)	Satisfied with her activities (1) Stays scared (1) How he does things is important (1)	Enjoys doing UA (1) I know him (1)
Comparison: Other Children (3)	0	1	2
Reasons		From early I could see there was something wrong – but she is now keeping up with others (1)	Compare other children's feelings (1) Monitor development (1)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Too young to share feelings – need to be there and think for him (1) If unable to play it would imply a problem (1) UA are important for learning (1)	Monitor progress (1) Important to play with others – upset, frustrated and angry if unable (1) Needs to attend school to learn, play and feel like other children (1)	Monitor child's activity and ability to play (1) UA are the most meaningful things for a child (1) Learn through play (1) If unable to play he would be house-bound. Need to get used to other children to socialize and one learns through play (1)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-20 Description of Answers for UA Dimension for Children Aged 3-4 years

3-4 years	**AI**	**CI**	**TD**
UA :3* (5)	1	4	0
Reason for answer	Not playing or walking well (1)	Same as others (1) No problem playing (2) Attends school, loves playing and being with friends. We accommodate her and her environment includes her (1)	
Observable behaviour	Not playing (1)	Playing well (3) Attends school (1) Interacts with family and friends (1) Same ability as others her age (1)	
UA :2 *(1)	1	0	0
Reason for answer	Tires quickly (1)		
Observable behaviour	Plays for a short time (1)		
UA : 1* (6)	2	0	4
Reason for answer	Always participates (1) No problem with UA he is hampered now as he is in hospital (1)		Attends school and playing (3) Likes to be with family and friend (2) Learns with play (1)
Observable behaviour	Loves playing (1) Hospitalised (1)		Playing well (4) Attends school (3)
Alternate items	Play only (3) Cognition (1) Schooling (1) Socializing (1)	Play only (2) Socializing (1)	Play only (2)

Comparison: Normal Behaviour (4)	2	1	1
Reasons	Unique (1) More active than other children – learns faster (1)	Ideally look at her (1)	No problem with achieving tasks (1)
Comparison: Other Children (8)	2	3	3
Reasons	Perform similarly to others (2)	Does everything – just slower (1) He is on par (1) Playing like others (1)	Ensure he is doing well (1) Monitor development (1) Playing like others (1)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Her ADLs have changed since hospitalisation (1) Play is important (2) Help if there is something wrong (1) Feel lonely and sad if not able to participate (1)	Frustrating and distressing to her not to be able to do UA (1) Indicates brain development; play develops personality and social skills (1) Play and school enables learning (1) Due to lack of mobility it is important to include her for her to develop self-acceptance (1) Learn through play (1)	Enjoys playing and participating with family. No close friendships at this stage (1) Important to play and socialise (1) Must attend school to learn (1) Socialize and keep up with friends through learning and play (1)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-21 Description of Answers for UA Dimension for Children Aged 4-5 years

4-5 years	**AI**	**CI**	**TD**
UA :3* (1)	1	0	0
Reason for answer	Unable to go to school when fitting. When in hospitalised unable to do UA (1)		
Observable behaviour	Fitting and weakness (1)		
UA :2* (2)	1	1	0
Reason for answer	Hospitalised (1)	No special school in Paarl. Communication is difficult with poor hearing. She likes games but struggles.	
Observable behaviour	Can't go to school or visit family or friends because he is hospitalised (1)	Communication difficulties and struggles with gross motor function (1)	
UA : 1* (9)	2	3	4
Reason for answer	Playing nicely; unable to go to school due to hospitalisation (1) No problem doing her UA – none of these are hers though (1)	Made friends and playing well (1) Wants to be involved everywhere (1) Doesn't require help with anything (1)	No problems (1) He is developing hobbies, loves sport and goes to school (1) Loves school &play (1) Doing everything normally (1)
Observable behaviour	Playing well (1) Doing her UA (1)	Playing well (1) Involved everywhere (1) Independent UA (1)	Chooses what he wants to play (1) Goes to school; plays cricket and rugby (1) Loves school; play (1) Doing everything well (1)

Alternate items	Eating (1) Playing only (1)	School (1) Playing only (1) Communication (1)	
Comparison: Normal Behaviour (9)	4	2	3
Reasons	Well before seizures (1) Concerned about him (1) All children are different (1) She is different; we monitor her improvement (1)	Not fond of school or homework (1) With his condition we need to look at him (1)	Limited exposure to other children (2) He is normal now so I need to think of his health to know if anything changes (1)
Comparison: Other Children (3)	0	2	1
Reasons		Compare her to help her reach that level (1) Compare to children in the community (1)	Playing the same as others; speech is slower (1)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Doctors must help if there are problems (1) To know if he can play (1) Every child need to go to school, learn and play with others (1) Monitor her development(1)	Important (1) Play makes him happy (1) Play indicated level of thinking, intelligence (1). Play teaches sharing, communication and learning (1) Playing and learning impacts your health and emotions (1)	If unable to do UA it will imply that something is wrong (2) Important for learning (1) Independence (1)

Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-22 Description of Answers for UA Dimension for Children Aged 5-6 years

5-6 years	**AI**	**CI**	**TD**
UA :3* (4)	2	1	1
Reason for answer	Can't play (1) After the accident unable to do this (1)	Not listening at school – bad behaviour. Likes to play (1)	Not allowed to go to school and can't play with friends (1)
Observable behaviour	Tires with playing and sport. Not going to school or playing as hospitalised (1) Unable (1)	Not listening at school (1)	Out of school and unable to play (1)
UA :2* (5)	2	2	1
Reason for answer	Asking to be with family and friends and to play (1) Needs more help at school; struggling to play with others (1)	Not going to school or playing sport. Plays on own (1) No longer at school as he got sick too often. Tires with play (1)	Some problem with school as she gives up easily with schoolwork and doesn't like homework (1)
Observable behaviour	Unable to play or visit family or friends as hospitalised (1) Needs help at school and struggles to play (1)	No schooling or sport (1) Plays alone (1) No schooling (1) Tires with play (1)	Gives up easily at school and doesn't like homework (1)
UA : 1* (3)	0	1	2
Reason for answer		Plays, talks and goes to school with no problem	Competent and keen to participate (1) Enjoys socializing and playing and going to school (1)
Observable behaviour		Plays and goes to	Competent (1)

		school (1)	Socializing, playing and going to school (1)
Alternate items	-	-	-
Comparison: Normal Behaviour (9)	4	3	2
Reasons	Enjoyed playing and being with family before (1) Struggling (1) Not able to do what other children are (1) Different to others (1)	Behaviour is different to others (1) Other children are at school, running and playing (1) Asthma varies everyday (1)	Huge range in progress between children (1) Before the burn she was playing and going to school.
Comparison: Other Children (3)	0	1	2
Reasons		Same as other 5 year olds (1)	Ensure she is doing the same as friends (1) Lacks self-confidence in comparison (1)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Socialization and relationships are important (1) Needs to play and go to school (2) Affects caregiver more than child. She doesn't know she is different (1)	Unknown (1) Parents should know (1) He is excluded and it frustrates him (1) Important for child (1)	Being unable to participate frustrates her and impact her emotional state (1) Monitor development. If house-bound it affects her mood negatively (1) Important for mental state, learning, emotions, gross motor and fine motor skills (1) Child's right to go to

			school – parent must ensure she goes to school (1)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-23 Description of Answers for UA Dimension for Children Aged 6-7 years

6-7 years	**AI**	**CI**	**TD**
UA :3* (3)	1	0	0
Reason for answer	Hospitalized – can't do anything (1)		
Observable behaviour	Unable to run, play or do sport (1)		
UA :2* (1)	0	1	0
Reason for answer		Doesn't do sport at school because of her liver (1)	
Observable behaviour		Doesn't play sport (1)	
UA : 1* (10)	3	3	4
Reason for answer	I facilitate all of these activities – everything is play for him (1) The hospital is very supportive, she goes to school here, plays with volunteers and other children. She has all her toys here and rides her bike (1) Always goes to school except today (1)	He does everything – nothing stops him (1) Always running and playing and had sports day at school (1) He participates well (1)	Plays, school and everything (1) Participates in everything (1) Wants to do everything with other children (1) Plays a lot (1)
Observable behaviour	Plays well (1) Goes to school and plays well (1)	Does everything (1) Running & playing (1) Participates well (1)	Participates in everything (3) Plays (1)

Alternate items	Play only (1)	-	-
Comparison: Normal Behaviour (6)	2	3	1
Reasons	Plays uniquely – judge him on that (1) She is good enough for him (1)	Accept him (1) Not normal compared to others – slower at school and sport (1) Limited interaction with other children	Needs to make up her own mind and participate (1)
Comparison: Other Children (6)	2	1	3
Reasons	Unable to perform as others and it upsets her (1) Monitor development (1)	Compared to others he has problems with sport (1)	Playing like others (1) The schooling system is such that you have to fit certain parameters (1) Monitor development (1)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Even if he can't walk – he can play – he needs to know he has some ability (1) It makes her happy (10 She gets upset because she can't participate like other children (1) Monitor him (1)	Feels excluded not being able to play at school (1) Affects parent more than child (2) Affect child negatively not being able to participate like other children (1) If unable to participate it may indicate an underlying health condition (1) Frustration at not doing what friends	Important (1) What is expected for them to fit in and be accepted at school and with peers (1) Could indicated illness for which you should seek help (2) Disappointment if unable to do UA (1)

		can. Extra work to stay intellectually on par if unable to go to school (1)	
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

10.7.4 Pain and Discomfort Dimension

Table 10-24 Description of Answers for PD Dimension for Children Aged 0-1 years

0-1 years	**AI**	**CI**	**TD**
PD :3* (1)	1	0	0
Reason for answer	Lots of pipes and pain from operation (1)		
Observable behaviour	Crying, frown, pulls still, lying still and not responding to play (1)		
PD :2* (5)	2	2	1
Reason for answer	Definitely in pain (1) You can see (1)	Cries in her sleep and restless (1)	Some discomfort with winds (1)
Observable behaviour	Grumpy, fidgeting, quivering lip, pinching eyes closes, shakes arms, pulls stiff, different cry (1) Crying and still (1)	Cries, restless, doesn't sleep well, fidgety, pulls a face (1)	Cries in a certain way, pulls face, turns red, pulls mouth, arches back (1)
PD : 1* (7)	1	3	3
Reason for answer	He is not crying (1)	Awake now, now has pain when she has a seizure (1) If he is in pain he cries and he is fine now (1) He can't cry so if he has pain I don't know and can't know (1)	Sleeping peacefully (1) She is herself, playing and moving about (1) Teeth are not coming out – so no pain (1)
Observable behaviour	Happy, not crying, wants to play (1)	Awake and seizure free (1) Not crying (1) I can't see anything different in him (1)	Peaceful and not crying (1) Not crying or holding her body as though it is sore (1) Not crying (1)

Alternate items	Add Descriptions of PD	Add Descriptions of PD	-
Comparison: Normal Behaviour(11)	3	4	4
Reasons	Monitor improvement (1) Children are all different (1) He was healthy before he got sick (1)	Aware of behaviour when not in pain (1) Know my child (1) No change in him (1)	I know her behaviour and if she is in pain (1) Cries and doesn't stop there is something wrong (1) A parent must learn your child's cries and mannerisms (1)
Comparison: Other Children (1)	1	0	0
Reasons	Cries just like other children (1)		
Importance for HRQoL: Yes (11)	4	3	4
Reasons	Help him and improve HRQoL (1) Help for the future to know what to expect with you child and therefore solve their problem (1) Seek help (2)	Help decrease PD (1) Help as pain makes her uncomfortable and move less (1) Help so that he can play and be happy (1)	If in pain he won't sleep or eat and cry all the time (1) Seek help (3) If in pain – won't eat or play and constantly cry all (1) If in pain- won't eat and lose weight (1)
Importance for HRQoL: NO (1)	0	1	0
Reasons		He can't let us know if he has pain – nothing changes (1)	

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-25 Description of Answers for PD Dimension for Children Aged 1-2 years

1-2 years	**AI**	**CI**	**TD**
PD :3* (0)	0	0	0
PD :2* (2)	2	0	0
Reason for answer	Verbalises pain when touched (1) He is sick (1)		
Observable behaviour	Verbalises, doesn't want to be touched, lies still; pulls a face (1) Cries, doesn't sleep well; becomes weak (1)		
PD : 1* (9)	1	4	4
Reason for answer	He is a nice child (1) Comfortable (1)	Only wheezing (1) Happy (1) If in pain he is grumpy and wants to be with me (1) No pain (1)	She is happy (1) Didn't complain, smiling (1) Happy and didn't complain (1) Doesn't have pain or sickness
Observable behaviour	Not crying (2) Playing (1)	Wheezing (1) Not crying (1) Content (2)	Happy not crying (1) Didn't complain (3) Happy (2) Smiling (1) Not crying (3)
Alternate items	Pain only (1)	Pain only (1)	-
Comparison: Normal Behaviour (11)	3	4	4
Reasons	Not normally in pain (1) Compare one day to another (1)	I know what the chest sounds are (1) We know what his problem is and how	Aware of her signs when in pain (1) Children are all different (2)

	When in pain he can't play – different from others (1)	he reacts (1) I know my child (1)	I can see if she changes (1)
Comparison: Other Children (1)	1	0	0
Reasons	Looks like other children (1)		
Importance for HRQoL: Yes (11)	3	4	4
Reasons	Seek help (1) Keep pain to minimum (1) We must know (1)	Seek help (3) Learn about his pain – life would be bad if always in pain (2)	If in pain unable to play or be happy (1) If in PD you are not healthy and it stops you exploring and developing as children can only focus on now (1) Hamper development (1) Ascertain if there is something bothering child (1)
Importance for HRQoL: NO (1)	1	0	0
	Unknown (1)		

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-26 Description of Answers for PD Dimension for Children Aged 2-3 years

2-3 years	**AI**	**CI**	**TD**
PD :3* (1)	1	0	0
Reason for answer	Had an operation (1)		
Observable behaviour	Pulls legs up; pulls a face, screaming (1)		
PD :2* (4)	1	2	1
Reason for answer	After plasma-phoresis they had to drug him so that he could sleep (1)	She is sick so she must have PD (1) Wants to do things and can't (1)	Pain knowing that his mom is leaving in the morning (1)
Observable behaviour	Verbalise, crying, wet himself (1)	Sick (1) Cries (1)	Verbalises (1)
PD : 1* (7)	2	2	3
Reason for answer	Smiling, running and playing (1) Not crying like other days and verbalises pain (1)	Verbalises (2)	Verbalises (3)
Observable behaviour	Not crying (2)	Verbalises (2)	Verbalises (3) Happy (1) Not crying (1)
Alternate items	Play only	-	Include illness
Comparison: Normal Behaviour (11)	4	4	3
Reasons	Familiar with his behaviour (1) Unique individual (2) Every child is different (1)	If in pain she is quiet otherwise she is active (1) Knowledge of child's behaviour (2) Unique (1)	Knowledge of child's behaviour (3)
Comparison: Other Children (1)	0	0	1
Reasons			Aware of other

			children but know my child's equilibrium (1)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Pain affects sleep; playing and interaction with others (1) Pain indicates illness (1) Seek help (2)	Relevant (1) Always better to ask (1) Pain causes sadness and inactivity (1) Seek help (1)	Pain affects sleep, appetite, play and emotion (1) Pain hampers development (1) Seek help (3)
Importance for HRQoL: NO	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-27 Description of Answers for PD Dimension for Children Aged 3-4 years

3-4 years	**AI**	**CI**	**TD**
PD :3* (1)	1	0	0
Reason for answer	Coughing (1)		
Observable behaviour	Verbalises, sleeping more and crying (1)		
PD :2* (4)	2	0	2
Reason for answer	Drip in hand – it must be sore (1) Verbalises (1)		Throat is sore (1) Paining as he doesn't know his father (1)
Observable behaviour	Drip (1) Verbalise (1)		Verbalises (2)
PD : 1* (7)	1	4	2
Reason for answer	Verbalise (1)	Verbalise (2) Happy and playing (1) Happy and no fever (1)	Healthy (2)
Observable behaviour	Verbalise (1)	Happy (2) Playing (1) Verbalise (2)	Verbalises (2)
Alternate items	Pain Only (1)	Pain only (1)	-
Comparison: Normal Behaviour(12)	4	4	4
Reasons	Knowledge of child's behaviour (4) Expect pain after surgery (1)	Knowledge of child's behaviour (4)	Knowledge of child's behaviour (4)
Comparison: Other Children (0)	0	0	0
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Impact ability to perform other tasks (1)	Unpleasant (1) Affects concentration (1)	Pain affects mobility (1) Pain affects learning

	Pain is unpleasant (2) Seek help (2) Pain causes unhappiness and wouldn't allow school attendance; playing and running (1)	Seek help (1) Affects appetite (2) Affects play and social interaction (1)	(1) Pain affects play (3) Unpleasant (1)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-28 Description of Answers for PD Dimension for Children Aged 4-5 years

4-5 years	**AI**	**CI**	**TD**
PD :3* (0)	0	0	0
PD :2* (3)	1	1	1
Reason for answer	Sometimes cries and says he is in pain (1)	Discomfort with chest scar and dirty nappy (1)	Headache and stomach ache (1)
Observable behaviour	Verbalises (1)	Pulls top down and verbalises (1)	Verbalise; not eating; crying (1)
PD : 1*(9)	3	3	3
Reason for answer	Talkative and comfortable (2) No pain when touched (1)	Verbalises (2) Happy (1)	Verbalise (3)
Observable behaviour	Talkative and comfortable (2) No pain when touched (1)	Verbalises (2) Happy (1)	Slept well (1) Happy (1) Verbalise (3)
Alternate items	Pain only	-	Pain only
Comparison: Normal Behaviour(12)	4	4	4
Reasons	Knowledge of child's behaviour (3) Never had pain before (1)	All children are different (2) Knowledge of child's behaviour (2)	Knowledge of child's behaviour (4)
Comparison: Other Children (0)	0	0	0
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Seek help (4) Affects play (1)	Always assume children with disability are suffering and have pain but it is not true he is happy (1)	Understand child and their pain (1) Seek help (3) Affect UA and learning (1)

		Affects life (1) Seek help (2) Pain brings sadness (1) Affects going to school, playing and emotional well-being (1)	
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-29 Description of Answers for PD Dimension for Children Aged 5-6 years

5-6 years	**AI**	**CI**	**TD**
PD :3* (1)	0	0	1
Reason for answer			Painful after burn (1)
Observable behaviour			Verbalise (1)
PD :2* (3)	1	2	0
Reason for answer	Restless after surgery (1)	Ear problem and can't cough (1)	
Observable behaviour	Restless & verbalising	Can't cough (1)	
PD : 1* (9)	3	3	3
Reason for answer	Verbalise (2) Not on medication (1) Active (1)	Verbalise (2) Playing (1)	Verbalise (3)
Observable behaviour	Verbalise (2) Active (1)	Verbalise (2) Playing (1)	Verbalise (3)
Alternate items	-	-	-
Comparison: Normal Behaviour(12)	4	4	4
Reasons	Old enough to verbalise pain (3) Knowledge of child's behaviour (2)	Knowledge of child's behaviour (3) When in pain he hurts himself and cries (1)	Knowledge of child's behaviour (3) Verbalise pain (1) Limited interaction with other children (1)
Comparison: Other Children (0)	0	0	0
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Seek help (4) Scared and not wanting to perform tasks (1)	Seek help (4) Affects UA; mobility and emotions (1)	Impacts emotion and mobility (1) Affect UA (3) Seek help (2)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-30 Description of Answers for PD Dimension for Children Aged 6-7 years

6-7 years	**AI**	**CI**	**TD**
PD :3* (0)	0	0	0
PD :2* (1)	0	1	0
Reason for answer		Stomach pain and moody (1)	
Observable behaviour		Moody (1)	
PD : 1*(11)	4	3	4
Reason for answer	Verbalise (4)	Verbalises (3)	Verbalise (4)
Observable behaviour	Verbalise (4) Happy (1)	Verbalises (3)	Verbalise (4)
Alternate items	Pain only (1)	-	Pain only (1)
Comparison: Normal Behaviour(12)	4	4	4
Reasons	Knowledge of child's behaviour (4)	Every child is different (2) Knowledge of child's behaviour (2)	Knowledge of child's behaviour (4)
Comparison: Other Children (0)	0	0	0
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Seek help (2) Affects eating, walking and emotion (1) Affects talking, playing, socializing (1) Want her to be happy (1)	Seek help (2) Affects concentration and eating (1) Affects mobility; SC and sport (1) Affects play (2)	Seek help (2) Affects play and socializing (2)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

10.7.5 Worried, Sad and Unhappy Dimension

Table 10-31 Description of Answers for WSU Dimension for Children Aged 0-1 years

0-1 years	**AI**	**CI**	**TD**
WSU :3* (0)	0	0	0
WSU:2* (2)	1	0	1
Reason for answer	Unhappy (1)		Sometimes WSU as hungry (1)
Observable behaviour	Fidgets; irritated and crying (1)		
WSU: 1* (6)	3	4	3
Reason for answer	Happy (1) Laughing (1) Playing (1)	Guessed (1) Happy (1) Smiling (1) Doesn't show any difference as he doesn't know what is happening because he can't hear or see (1)	Content (1) Smiling (1) Happy (1) Playing (1) Has food (1)
Observable behaviour	Happy (1) Laughing (1) Playing (1)	Happy (1) Smiling (1) None (2)	Content (1) Smiling (1) Happy (1) Playing (1)
Alternate items	Remove Dimension (1)	Remove Dimension (2)	Remove Dimension (2) Growth (1) Eating (1) Sleeping (1) Cognition (1)
Comparison: Normal Behaviour (9)	3	4	2
Reasons	Knowledge of child's behaviour (3)	Unknown (1) Different from others (2) Knowledge of child's behaviour (1)	Knowledge of child's behaviour (2)

Comparison: Other Children (3)	1	0	2
Reasons	Busy like other children		Unknown (1) Each child shows different emotions and good to look at everyone (1)
Importance for HRQoL: Yes (7)	3	2	2
Reasons	Seek help (3) Non-verbal thus caregiver must know signs (1)	Seek help (2)	Not good for Health – but will affect the child more when they are older (1) Affects the parent more than the child (2)
Importance for HRQoL: NO (5)	1	2	2
Reasons	Not important as child is too young (1)	Too young to feel WSU (2)	Too young to feel WSU (2)

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-32 Description of Answers for WSU Dimension for Children Aged 1-2 years

1-2 years	**AI**	**CI**	**TD**
WSU :3* (0)	0	0	0
WSU:2*(2)	2	0	0
Reason for answer	Worries when he sees doctors or nurses (1) He must be worried and unhappy he is sick (1)		
Observable behaviour	Crying (1) Not playing (2)		
WSU: 1* (10)	2	4	4
Reason for answer	I am worried; I don't know if he is worried (1) She is playing well (1)	Happy (2) Playing (1) Excited (1) Vocalises (1)	Happy (3) Smiling (1)
Observable behaviour	Unknown (1) Playing (1)	Happy (2) Playing (1) Excited (1) Vocalises (1)	Happy (3) Smiling (1)
Alternate items	Remove Sad (1)	-	Remove sad (1) Remove worry (1)
Comparison: Normal Behaviour(11)	4	3	4
Reasons	Enjoys playing (1) Not normally worried (2) Unique (1)	Has his own feelings (1) Unique (1) Knowledge of child's behaviour (1)	Knowledge of child's behaviour (4)
Comparison: Other Children(1)	0	1	0
Reasons		Compare to other children with asthma (1)	

Importance for HRQoL: Yes (12)	4	4	4
Reasons	He likes to play (1) Unknown (1) Learn about child (1) Seek help (1)	Seek help (1) Learn child's behaviour (1)	Indicates a problem (1) Hampers playing, learning and development (1) Not able to verbalise; we must know when there is something wrong (1) Seek help (2)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-33 Description of Answers for WSU Dimension for Children Aged 2-3 years

2-3 years	**AI**	**CI**	**TD**
WSU :3* (1)	1	0	0
Reason for answer	Always unhappy: can't play, can't see and frustrated (1)		
Observable behaviour	Moody, nags, kicks restless, frustration (1)		
WSU:2* (4)	1	1	2
Reason for answer	In between: happy and then cries to go home (1)	Sometimes sad (1)	Worry pot and anxious (1) A bit sad (1)
Observable behaviour	Cries (1)	Cries, sleeps and puts hands in front of face (1)	Verbalise, asks lots of questions and fights (1) Cries when I leave (1)
WSU: 1* (7)	2	3	2
Reason for answer	Happy (1) Playing (1)	Healthy (1) Happy when mom is around (1) Happy (1)	Not appropriate he is too young (1) Happy child (1)
Observable behaviour	Happy (1) Playing (1)	Healthy (1) Happy (2)	
Alternate items	-	-	Remove Dimension (1) Remove worry (1)
Comparison: Normal Behaviour(11)	4	4	3
Reasons	Happy before hospitalisation (1) Individual (1)	Healthy (1) Knowledge of child's behaviour (3)	Knowledge of child's behaviour (3)
Comparison: Other Children (1)	0	0	1
Reasons			I don't think his anxiety is out of

			normal so I compare him to know if we need to seek help (1)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Monitor health (1) Indicates illness (2) Unpleasant (1)	Indicated general health (1) Seek help (2) Affects play (2) Affects mobility and development (1)	Important when older; not now (3) Affects UA (1) Not good to have sustained negative emotions (1)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-34 Description of Answers for WSU Dimension for Children Aged 3-4 years

3-4 years	**AI**	**CI**	**TD**
WSU :3* (1)	0	0	1
Reason for answer			Gets upset when I go to work (1)
Observable behaviour			Cries, angry (1)
WSU:2* (0)	0	0	0
WSU: 1* (11)	4	4	3
Reason for answer	Talking, running, jumping & playing (1) Hasn't complained (1) Happy (1)	Himself – chatty & asking questions (1) Happy (2) Excited (1)	Happy (3)
Observable behaviour	Talking, running, jumping & playing (1) Verbalises (1) Happy (1)	Chatty (1) Happy (2) Excited (1)	Happy (3)
Alternate items	-	Remove worry	-
Comparison: Normal Behaviour(10)	3	3	4
Reasons	Knowledge of child's behaviour (3)	All children are different (1) Knowledge of child's behaviour (2)	Knowledge of child's behaviour (4)
Comparison: Other Children (5)	1	4	0
Reasons	Unknown (1)	Compare to others as a guide (1)	
Importance for HRQoL: Yes (11)	3	4	4
Reasons	Knowledge of child's behaviour (3)	Unpleasant (3) Seek help (1)	Seek help (1) Not good (2) Affects UA (1)
Importance for HRQoL: NO (1)	1	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-35 Description of Answers for WSU Dimension for Children Aged 4-5 years

4-5 years	**AI**	**CI**	**TD**
WSU :3* (2)	2	0	0
Reason for answer	Asking for school (1) Asking to go home (1)		
Observable behaviour	Verbalises (2) Crying (1)		
WSU:2* (2)	0	1	1
Reason for answer		Wants to go home (1)	Missing his father (1)
Observable behaviour		Vocalises (1)	Vocalises (1)
WSU: 1* (8)	2	3	3
Reason for answer	Going home (1) She is used to the hospital staff (1)	Happy (1) Vocalises (2) Smiling (1)	Only sad if he doesn't get what he wants (1) Vocalises (2)
Observable behaviour	Vocalises (1) Chatty (1)	Happy (1) Vocalising (2) Smiling (1)	Vocalises (2)
Alternate items	-	Remove worry (1)	Ask if happy (1)
Comparison: Normal Behaviour(11)	4	4	3
Reasons	Children are all different (1) Knowledge of child's behaviour (3)	Knowledge of child's behaviour (4)	Knowledge of child's behaviour (3)
Comparison: Other Children (1)	0	0	1
Reasons			I know when children are anxious or sad (1)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Inform doctors(1) Unknown (1) Seek help (2)	Indicates illness (1) Seek help (1) Affects health (2)	Affects play (3) Affects development(2) Not good for child (1)

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-36 Description of Answers for WSU Dimension for Children Aged 5-6 years

5-6 years	**AI**	**CI**	**TD**
WSU :3*	1	1	1
Reason for answer	Scared for operation (1)	Unhappy (1)	Worried about scaring of leg (1)
Observable behaviour	Crying (1)	Unhappy (1)	Crying & vocalises (1)
WSU:2* (1)	1	0	0
Reason for answer	Not allowed to play on floor in hospital (1)		
Observable behaviour	Not able to play (1)		
WSU: 1* (8)	2	3	3
Reason for answer	Happy and smiling (1) Not worried (1)	Hyperactive (1) Happy (2)	Happy (3)
Observable behaviour	Happy and smiling (1) Not worried (1)	Hyperactive (1) Happy (2)	Happy (3)
Alternate items	Remove unhappy (1)	-	Remove worry (1)
Comparison: Normal Behaviour(11)	3	4	4
Reasons	Vocalises emotions (1) Knowledge of child's behaviour (3)	Individual (2) Knowledge of child's behaviour (2)	Knowledge of child's behaviour (4)
Comparison: Other Children (1)	1	0	0
Reasons	When other children want something they are also sad (1)		
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Seek help (2) Affects play (1) Deserves happiness (1)	Unknown (1) Needs to be positive to get better (1) Pain decreases QoL (2)	Indicates wellness (1) Seek help (1) Affects behaviour (1)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

Table 10-37 Description of Answers for WSU Dimension for Children Aged 6-7 years

6-7 years	**AI**	**CI**	**TD**
WSU :3* (2)	1	1	0
Reason for answer	Worried and unhappy about the boy next door who is not well (1)	Wants to stay with grandmother (1)	
Observable behaviour	Quiet; withdrawn (1)	Verbalises (1)	
WSU:2* (3)	1	0	2
Reason for answer	Worried about having blood taken; wants to go home (1)		Worried about me coming to work (1) Worried about school; unhappy at getting reprimanded at school (1)
Observable behaviour	Vocalises (1)		Crying (2) Misbehave, short-temper, screaming (1)
WSU: 1* (7)	2	3	2
Reason for answer	Happy (2)	Happy (1) Frustrated; not worried (1) Happy to see his physio and doctors (1)	Happy (2) Laughing (1) Playing (1)
Observable behaviour	Happy (2)	Happy (2) Not worried (1) Vocalises (1)	Happy (2) Laughing (1) Playing (1)
Alternate items	-	-	-
Comparison: Normal Behaviour(10)	3	4	3
Reasons	Knowledge of child's behaviour (3)	Individual (2) Monitor behaviour changes (2)	Individual (2) Monitor improvement (1)
Comparison:	1	0	1

Other Children (2)			
Reasons	Compare as a guide (1)		Guide for emotional development (1)
Importance for HRQoL: Yes (12)	4	4	4
Reasons	Withdrawn (1) Unpleasant (1) Seek help (2)	Affects family more than child (1) May affect him later in life; not now (1) He gets worried about running out of medication and doing his physio (1) Affects self-confidence (1)	Decreased QoL (1) Seek help (2) Affects overall functioning (2)
Importance for HRQoL: NO (0)	0	0	0

1 No problem in dimension; 2* some problems in dimension; 3* A lot of problems in dimension*

10.8 Appendix 8 Delphi Study Informed Consent

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Informed consent for Item pool generation of new HRQoL measure

Information Sheet

Title of the Study: Development of an English Health-Related Quality of Life measure for children under seven years of age, derived from the EQ-5D-Y, to be completed by proxy.

Dear Participant,

I am developing a new HRQoL measure for children under the age of seven years as part of my PhD in physiotherapy at the University of Cape Town. After review of the literature I identified the need to develop a new proxy Health-Related Quality of Life (HRQoL) measure based on observable behaviour as set out in the Food and Drug Association (FDA) guidelines.

The EuroQoL stable of measures is cited as the most used adult measure and has considerable clinical utility. The Youth version of the measure has been widely used since its creation in 2010. EuroQoL are currently developing a utility index for the Youth Measure. The measures have a well-accepted definition of HRQoL with five comprehensive dimensions. A proxy measure for young children would add value to this measure and allow comparison of HRQoL over the life span.

After cognitive interviews with 84 caregivers of typically developing, acutely-ill and chronically-ill children a preliminary item bank has been created. Items were also included from extensive literature reviews.

We would like to ask you to contribute to this item bank with your expert knowledge in the field of HRQoL and/or child health.

We would like to conduct a Delphi study with two rounds, of no longer than 15 minutes each, in the month of May 2016. If you are willing and available to participate in the study we ask you to please complete and return the informed consent to us by no later than 31 March 2016.

Your participation in the study is voluntary and there will be no consequences for not completing the study. Members of the Delphi panel will remain anonymous. Your contribution will be kept anonymous and the raw data will only be available to me and my supervisor, Prof Jennifer Jelsma.

There are no risks in taking part in this study. You will unfortunately not be reimbursed for your time. The benefits of your contribution will be far reaching and if the measure is validated you will have access to a new HRQoL measure in your practice.

Thank you, for your time in considering being a member of this Delphi Panel.

If you have any questions or concerns about the study you may contact the researcher or the supervisor:

Researcher

Janine Verstraete

Red Cross War Memorial Children's Hospital

Division of Physiotherapy

S13 Out Patients Building

Klipfontein Road

Rondebosch

Tel: 021 658 5033

Cell: 082 840 9293

Supervisor

Professor J. Jelsma

University of Cape Town

Department of Health &Rehabilitation Sciences

Division of physiotherapy

F45 Old Main Building

Groote Schuur Hospital

Observatory

Tel: 021-406 6401

If you have any queries about your rights or welfare as a research participant please contact;

Professor M. Blockman

The University of Cape Town

Faculty of Health Sciences Human Research Ethics Committee

Tel: 021 406 6492

Room: E52.24 Old Main Building

Consent Form

Please can you read through the table below and mark off your answer with an X

Declaration	Yes	No
I have read through the information provided and understand it.		
I understand that my consent is required.		
I understand that it is my choice to take part and I can refuse my consent without any consequences.		
I understand that not agreeing to take part in the study will not change my professional interaction with the researcher in any way.		
I understand that my identity will remain anonymous.		
I consent to taking part in this research of my own free will.		

Signed:

Participant's signature Date

Researcher signature Date

10.9 Appendix 9 Content Validity Index Template

Item	1 not relevant	2 somewhat relevant	3 quite relevant	4 highly relevant

Additional Items:

_____
_____
_____
_____
_____
_____
_____

10.10 Appendix 10 Delphi Round One

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Health Related Quality of Life (HRQoL) measure for very young children - item pool generation

1.

Informed consent for Item pool generation of new HRQoL measure

Information Sheet

Title of the Study: Development of an English Health Related Quality of Life instrument for children under three years of age, derived from the EQ-5D-Y, to be completed by proxy.

Dear Participant,

I am developing a new HRQoL instrument for children under the age of three years as part of my PhD in physiotherapy at the University of Cape Town. After review of the literature I identified the need to develop a new proxy Health Related Quality of Life (HRQoL) measure based on observable behaviour as set out in the Food and Drug Association (FDA) guidelines.

The World Health Organization Quality of Life Assessment (WHOQOL) group defines Quality of Life (QoL) as "individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. Health Related Quality of Life (HRQoL) can be considered a sub-group of QoL, which can be measured by the impact the subjective perception of physical, emotional, mental and social functioning has on QoL.

The EuroQoL stable of instruments are cited as the most used adult instrument and has considerable clinical utility. The Youth version of the instrument has been widely used since its creation in 2010. The measures have a well-accepted definition of HRQoL with five comprehensive domains. A proxy measure for young children would add value to this measure and allow comparison of HRQoL over the life span.

After cognitive interviews with 84 caregivers of typically developing, acutely-ill and chronically-ill children a preliminary item bank has been created. Items were also included from extensive literature reviews.

We would like you to contribute to this item bank with your expert knowledge in the field of

HRQoL and/or child health.
We are conducting a Delphi study with two rounds, of no longer than 15 minutes each.

Your participation in the study is voluntary and there will be no consequences for not completing the study. Members of the Delphi panel will remain anonymous. Your contribution will be kept anonymous and the raw data will only be available to myself and my supervisor, Prof Jennifer Jelsma.

There are no risks in taking part in this study. You will unfortunately not be reimbursed for your time. The benefits of your contribution will be far reaching and if the instrument is validated you will have access to a new HRQoL measure in your practice.

Thank you, for your time in considering being a member of this Delphi Panel.

If you have any questions or concerns about the study you may contact the researcher or the supervisor:

Researcher	Supervisor
Janine Verstraete	Professor J. Jelsma
Red Cross War Memorial Children's Hospital	University of Cape Town
Division of Physiotherapy &Rehabilitation Sciences	Department of Health
S13 Out Patients Building	Division of physiotherapy
Klipfontein Road	F45 Old Main Building
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Tel: 021 658 5033	Observatory
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If you have any queries about your rights or welfare as a r

* 1. I have read through the information provided and understand it

Yes	No
○	○

2

* 2. I understand that my consent is required

Yes	No
◯	◯

* 3. I understand that it is my choice to take part and I can refuse consent without any consequences

Yes	No
◯	◯

* 4. I understand that not agreeing to take part in the study will not change my professional interaction with the researchers in any way.

Yes	No
◯	◯

* 5. I understand that my identity will remain anonymous

Yes	No
◯	◯

* 6. I consent to taking part in the research of my own free will

Yes	No
◯	◯

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Health Related Quality of Life (HRQoL) measure for very young children - item pool generation

2.

* 7. The following items could be included in a Health Related Quality of Life (HRQoL) measure. Could you please rate their relevance for HRQoL in children for each of the corresponding age brackets

	0-12 Months	12-24 Months	24-36 Months
Behaviour			
Cognition			
Communication			
Dependence on care			
Dexterity			
Discomfort			
Dressing			
Eating (Able to take food orally)			
Energy			
Feeding (Ability of child to feed him/herself)			
Growth			
Hobbies			
Hygiene			
Immunizations			

	0-12 Months	12-24 Months	24-36 Months
Independence			
Kicking			
Learning			
Achievement of Milestones			
Mood			
Motivation			
Movement			
Pain			
Play			
Pre-School			
Pride			
Relationships			
Religion			
Routine			
Sad			
Self-care			
Self-Esteem			
Senses			
Sickness			
Sleeping			
Socializing			
Toileting			
Unhappy			
Upper limb Movement			
Usual Activities			
Walking			

* 11. With the proxy completion of the outcome measure, which recall period is most relevant when considering the HRQoL of a very young child.

- ◯ Today
- ◯ Current
- ◯ Yesterday
- ◯ Last Week
- ◯ Last Month
- ◯ Other

Please provide reasoning for your answer

Thank you, for the time taken to complete the survey.
A second round of the study will commence in June 2016

10.11 Appendix 11 Delphi Round Two

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Round 2: Health Related Quality of Life Measure for very Young Children - Item Pool Generation

Dear Participant,

Thank you for your participation in the first round of the Delphi study.
The results from the first round have been collated. The items have been scored according to a content validity index. All items which scored >0.75 have been included in the second round of item selection.

The aim of this round of the survey is to determine a final item bank for consideration of the development of the new instrument. Thus you will be asked to rank the items as well as suggest any possible overlap of items included. Your opinion of the wording for your top ranked items is also of utmost importance.

Thank you for your ongoing participation in this study. The study will close on the 29 July 2016. After all of the data analysis and development of the new instrument you will all be sent a report on the progress of the instrument.

Thank you, for your time in considering to participate in the second round of this survey.

If you have any questions or concerns about the study you may contact the researcher or the supervisor:

Researcher

Janine Verstraete

Red Cross War Memorial Children's Hospital

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S13 Out Patients Building

Supervisor

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* 1. Please indicate whether you agree to participate in the second round of the study or not.

- ◯ I agree to participate in the second round.
- ◯ I would not like to participate in the second round

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Round 2: Health Related Quality of Life Measure for very Young Children - Item Pool Generation

Items to be included for children aged 0-12 Months

2. These results reflect the items scoring a Content Validity Index (CVI) > 0.75 for the age group 0-12 months from the first round of the survey. Please rank only the top seven items (with 1 being the most important) to assess HRQoL in this age group.

	1	2	3	4	5	6	7
Eating (Able to take food orally)	○	○	○	○	○	○	○
Crying	○	○	○	○	○	○	○
Mood	○	○	○	○	○	○	○
Movement	○	○	○	○	○	○	○
Pain	○	○	○	○	○	○	○
Play	○	○	○	○	○	○	○
Relationships	○	○	○	○	○	○	○
Senses	○	○	○	○	○	○	○
Sickness	○	○	○	○	○	○	○
Sleeping	○	○	○	○	○	○	○
Unhappy	○	○	○	○	○	○	○
Upper limb Movement	○	○	○	○	○	○	○

3. Please state which items from the list overlap. If the items could be combined which label should they be given.

4. Please comment if there are any item/s which you feel need to be included in the instrument for children aged 0-12 months that are not reflected in the list. Please justify why the item/s should be included

4

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Round 2: Health Related Quality of Life Measure for very Young Children - Item Pool Generation

Items to be included for children aged 0-12 Months

5. Please state why you choose each of your top ranked items for children aged 0-12 months

Eating (Able to take food orally)	
Crying	
Mood	
Movement	
Pain	
Play	
Relationships	
Senses	
Sickness	
Sleeping	
Unhappy	
Upper limb Movement	

6. What descriptors would you use for your top seven ranked items? An example of a descriptor for the item self-care, would be: able to wash hands, face and indicate toileting needs.

Eating (Able to take food orally)	
Crying	
Mood	
Movement	
Pain	
Play	
Relationships	
Senses	
Sickness	
Sleeping	
Unhappy	
Upper limb Movement	

7. These results reflect the items scoring a Content Validity Index (CVI) > 0.75 for the age group 12-24 months from the first round of the survey. Please only rank the top 7 items (with 1 the most important) to assess HRQoL in this age group.

	1	2	3	4	5	6	7
Eating (Able to take food orally)	○	○	○	○	○	○	○
Mood	○	○	○	○	○	○	○
Movement	○	○	○	○	○	○	○
Pain	○	○	○	○	○	○	○
Play	○	○	○	○	○	○	○
Relationships	○	○	○	○	○	○	○
Senses	○	○	○	○	○	○	○
Sickness	○	○	○	○	○	○	○
Sleeping	○	○	○	○	○	○	○
Unhappy	○	○	○	○	○	○	○
Upper limb Movement	○	○	○	○	○	○	○
Achievement of Milestones	○	○	○	○	○	○	○
Behaviour	○	○	○	○	○	○	○
Communication	○	○	○	○	○	○	○
Discomfort	○	○	○	○	○	○	○
Energy	○	○	○	○	○	○	○
Growth	○	○	○	○	○	○	○
Routine	○	○	○	○	○	○	○
Sad	○	○	○	○	○	○	○
Socializing	○	○	○	○	○	○	○
Usual Activities	○	○	○	○	○	○	○
Walking	○	○	○	○	○	○	○
Achievement of Milestones	○	○	○	○	○	○	○

8. Please state which items from the list overlap. If the items could be combined which label should they be given.

9. Please comment if there are any item/s which you feel need to be included in the instrument for children aged 12-24 months that are not reflected in the list. Please justify why the item/s should be included

9

10. Please state why you choose each of your top ranked items for children aged 12-24 months

Eating (Able to take food orally)	
Mood	
Movement	
Pain	
Play	
Relationships	
Senses	
Sickness	
Sleeping	
Unhappy	
Upper limb Movement	
Achievement of Milestones	
Behaviour	
Communication	
Discomfort	
Energy	
Growth	
Routine	
Sad	
Socializing	
Usual Activities	
Walking	
Achievement of Milestones	

11. What descriptors would you use for your top seven ranked items? An example of a descriptor for the item self-care, would be: able to wash hands, face and indicate toileting needs.

Eating (Able to take food orally)	
Mood	
Movement	
Pain	
Play	
Relationships	
Senses	
Sickness	
Sleeping	
Unhappy	
Upper limb Movement	
Achievement of Milestones	
Behaviour	
Communication	
Discomfort	
Energy	
Growth	
Routine	
Sad	
Socializing	
Usual Activities	
Walking	
Achievement of Milestones	

12. These results reflect the items scoring a Content Validity Index (CVI) > 0.75 for the age group 24-36 months from the first round of the survey. Please only rank the top 7 items (with 1 the most important) to assess HRQoL in this age group.

	1	2	3	4	5	6	7
Eating (Able to take food orally)	○	○	○	○	○	○	○
Mood	○	○	○	○	○	○	○
Movement	○	○	○	○	○	○	○
Play	○	○	○	○	○	○	○
Relationships	○	○	○	○	○	○	○
Senses	○	○	○	○	○	○	○
Sickness	○	○	○	○	○	○	○
Sleeping	○	○	○	○	○	○	○
Unhappy	○	○	○	○	○	○	○
Upper limb Movement	○	○	○	○	○	○	○
Behaviour	○	○	○	○	○	○	○
Discomfort	○	○	○	○	○	○	○
Energy	○	○	○	○	○	○	○
Growth	○	○	○	○	○	○	○
Routine	○	○	○	○	○	○	○
Sad	○	○	○	○	○	○	○
Socializing	○	○	○	○	○	○	○
Usual Activities	○	○	○	○	○	○	○
Walking	○	○	○	○	○	○	○
Cognition	○	○	○	○	○	○	○
Feeding (Ability of child to feed him/herself)	○	○	○	○	○	○	○
Independence	○	○	○	○	○	○	○
Learning	○	○	○	○	○	○	○
Worry	○	○	○	○	○	○	○

13. Please state why you choose each item in your top 5 responses

Eating (Able to take food orally)	
Mood	
Movement	
Play	
Relationships	
Senses	
Sickness	
Sleeping	
Unhappy	
Upper limb Movement	
Behaviour	
Discomfort	
Energy	
Growth	
Routine	
Sad	
Socializing	
Usual Activities	
Walking	
Cognition	
Feeding (Ability of child to feed him/herself)	
Independence	
Learning	
Worry	

14. Please state which items from the list overlap. If the items could be combined which label should they be given.

15. Please comment if there are any item/s which you feel need to be included in the instrument for children aged 24-36 months that are not reflected in the list. Please justify why the item/s should be included

16

16. Please state why you choose each of your top ranked items for children aged 24 - 36 months

Eating (Able to take food orally)	
Mood	
Movement	
Play	
Relationships	
Senses	
Sickness	
Sleeping	
Unhappy	
Upper limb Movement	
Behaviour	
Discomfort	
Energy	
Growth	
Routine	
Sad	
Socializing	
Usual Activities	
Walking	
Cognition	
Feeding (Ability of child to feed him/herself)	
Independence	
Learning	
Worry	

17. What descriptors would you use for your top seven ranked items? An example of a descriptor for the item self-care, would be: able to wash hands, face and indicate toileting needs.

Eating (Able to take food orally)	
Mood	
Movement	
Play	
Relationships	
Senses	
Sickness	
Sleeping	
Unhappy	
Upper limb Movement	
Behaviour	
Discomfort	
Energy	
Growth	
Routine	
Sad	
Socializing	
Usual Activities	
Walking	
Cognition	
Feeding (Ability of child to feed him/herself)	
Independence	
Learning	
Worry	

10.12 Appendix 12 Descriptor Suggestions from the Delphi Study

Table 10-38 Summary of the Importance of Behaviour and Suggested Descriptors per Age Group

Importance of Behaviour (12-24 months)	• Behaviour can be an indicator of good health and overlaps with pain. • Appropriate behaviour is strongly suggestive of a happy child. • Behaviour would indicate whether child is responding appropriately to stimuli.
Descriptors	• Behaviour appropriate to age. • Response to other people, environment and activities.
Importance of Behaviour (24-36 months)	• Poor health often presents with abnormal behaviour such as: shy, clingy or aggressive and disruptive. • Stable behaviour patterns suggest that children are comfortable with themselves.
Descriptors	• Behaviour appropriate to age.

Table 10-39 Summary of the Importance of Communication and Suggested Descriptors per Age Group

Importance of Communication (12-24 months)	• Any type of communication: smiling, crying, kissing the mother, wanting to stay with a person or not wanting to stay with a person, are necessary aspects of a child of this age. • Start of child's ability to express himself
Descriptors	• Able to use the body for communication (hugs, kisses, smiles, crying etc.) • Making needs known. • With family and the world.

Table 10-40 Summary of the Importance of Eating and Suggested Descriptors per Age Group

Importance of Eating (0-12 months)	• From the birth (until death) any person eats. If eating is not normal or absent it is a sign of something not working well. • Definite sensory pleasure in eating, in exploring the textures/taste etc. Particularly important when breastfed, in terms of mother-infant bonding (and good mom-baby relationship is obviously essential for an infant's QOL). • The ability to feed well is core to so many other functions in the new born. A source of huge stress to the caregiver if it's not going well. • Children who are not able to take in food orally or via feeding tube will have poorer health and quality of life. • Eating reflects appetite, and also reflects issues such as swallowing. • A child, who can take food in orally, will be healthy and content and hence have a better HRQoL. • One would die without food.
Descriptor	• 0-6 months: will and ability to suck milk. 6-12 months: curious toward food and able to take and taste pieces of food. • Able to suck and swallow/chew and swallow (age dependent) without reflux/aspiration. In older infants - able to finger feed solids and semi-solids. A negative score might provide the option of "gags when food is placed in mouth". • Able to feed comfortably without fatigue or fussiness. • Sustaining good nutritional intake, able to swallow well, starting to chew on food appropriately for age. • Able to take food orally. • Feeding related to age.
Importance of Eating (12-24 months)	• The ability of eating autonomously. • Essential to health wellbeing growth and development. • Essential for growth and development.
Descriptor	• Will and ability to eat autonomously, with cutlery (even if not used correctly) or with hands. • Able to finger feed a variety of foods and textures.
Importance of Growth (12-24 months)	• Growth is important indicator of good health. • Proper growth indicates child is healthy. • Shows progress.
Descriptor	• Growth and general well-being. • Putting on weight and increasing in height. • On normal growth parameters.

Importance of Eating (24-36 months)	• Self-feeding indicates dexterity and independence. • Essential for life.
Descriptor	• Able to feed themselves using at least a spoon, enjoying food and no difficulty with swallowing or retaining food. • Eat independently.
Importance of Growth (24-36 months)	• According to growth parameters.
Descriptor	• Parameter of growth chart.

Table 10-41 Summary of the Importance of Independence and Suggested Descriptors per Age Group

Importance of Independence (24-36 months)	• Independence is known to improve HRQoL in older groups, and is likely to be true in this population also. • As an indicator of good health and absence of severe physical disability. • At this age they are developing independence in a known environment. • By now they are able to do thing with certain independence.
Descriptors	• Able to eat independently; able to dress independently; able to go to the toilet independently; able to wash face independently. • Self-care activities. • Able to wash and dry hands, brush teeth with help and put on a T shirt. • Able to be left with carer.

Table 10-42 Summary of the Importance of Mood and Suggested Descriptors per Age Group

Importance of Mood (0-12 months)	• Forms the basis for a happy life. • This encompasses what is most important in QOL - if a child is sad/crying most of the time then QOL cannot be good, whereas a happy/smiling baby (regardless of disability/disease state) is finding satisfaction/happiness in their life and therefore has better QOL. • Mood indicates contentment and alertness and provides the basis for interaction with the caregiver and environment. • The general mood seems to be a good indicator of quality of life.
Descriptors	• Draws attention. • Mood items might have options of: "mostly content", "cries occasionally", "cries often". • Generally content, may be irritable when tired or hungry. • Generally cheerful and responsive, rarely irritable, no major fluctuations in mood.
Importance of Mood (12-24 months)	• A 12-24 month old child communicates with facial expressions, giving an idea of his mood. If he seems sad, this must mean something, small or big. If he smiles, this is a good sign. • Mood includes happiness/sadness. A mostly happy/contented mood would reflect general well-being. • Indicative of emotional well-being. • Fundamentally if a child is happy and responsive there is reasonable QoL.
Descriptors	• Being in a negative mood frequently. • Mostly content/happy; cries occasionally; cries often; inconsolable. • Generally content, expresses frustration and displeasure appropriately. • Mood stable, and generally content.
Importance of Mood (24-36 months)	• Mood reflects satisfaction with everyday life, one of the cornerstones of QOL. • It is difficult to have good QoL if you are depressed, lacking in energy or unhappy.
Descriptors	• Mostly content; unhappy some of the time; unhappy most of the time; inconsolable. • Generally content. • Cheerful and energetic with no inappropriate swings in mood.

Table 10-43 Summary of the Importance of Movement and Suggested Descriptors per Age Group

Importance of Movement (0-12 months)	• From birth until death any person moves; in different ways according to age. I suggest age specific movement specifications according to the child's age. • Early movement indicative of neurological and musculoskeletal health. • Good movement suggests that the person in pain free, and not limited by issues such as paralysis or orthopaedic problems. • Being able to move limbs freely would indicate a healthy child without a mobility problem and hence good HRQoL.
Descriptors	• 0-6 months: able to move arms and hands and legs and feet, and head, eyes, specific according to his age. 6-12 months: able to use arms and legs and head to explore, move from one place to another, to play with small object/toys. • Able to run around. • Movements smooth and functional. • Moving freely in age-appropriate fashion. Able to move all limbs without constraints. Using hands well. • Moving all four limbs freely.
Importance of Movement (12-24 months)	• Normal movement suggests an absence of pain and discomfort, and a toddler needs to move and explore.
Descriptors	• Able to move generally and freely without discomfort. Able to move and use hands particularly
Importance of Movement (24-36 months)	• Free appropriate movement suggests that there is little or no pain or discomfort and is related to independence
Descriptor	• Able to move freely, and without pain or discomfort; particularly moving hands and upper limbs well
Importance of Achievement of Milestones (24-36 months)	• This is an indicator of good health and absence of chronic conditions/ disability • A measurable way of monitoring progress
Descriptors	• No suggestion

Table 10-44 Summary of the Importance of Pain and Suggested Descriptors per Age Group

Importance of Pain (0-12 months)	• Pain is a message the body gives to alert us that it needs help. • The child will cry if in pain. From the birth even hunger is perceived with pain, hence he cries because he wants to eat (but in this case it is very difficult to identify pain and know what the cause is, because the child cannot explain it). Later pain becomes a more precise message for something which is not working well. As the child gets older he learns to explain where the pain is, helping the adult to understand and intervene. This item would need age specific descriptors. • Pain might have the greatest impact on HRQOL • Pain is known to detrimentally affect QOL, and the perception of pain is variable amongst different individuals. One would be remiss in excluding pain simply because infants cannot verbally express it. • Presence of pain has huge emotional and physiological spinoffs which affect all facets of well-being. • Chronic or acute pain is a useful indicator of health. Crying would be the symptom but you could also look at facial grimacing and general discomfort.
Descriptors	• 0-6 months: continuous and/or anomalous pain - e.g. colic is normal. 6-12 months: anomalous pain - e.g. pain to foot/hand or other parts of the body. • Having pain or discomfort. • Consider scale of "always", "often", "occasionally" or "never" in pain. • Daily activities not hampered by persistent or severe pain.
Importance of Pain (12-24 months)	• Pain is an index of something not going very well in the body. • Pain equates to an inability to interact with the environment appropriately, and is known to impact negatively on HRQoL. • Chronic pain is important indicator of poor health.
Descriptors	• Complaining of any pain. • In pain all of the time, most of the time; some of the time; never.
Importance of Pain (24-36 months)	• Pain as a general indicator of poor health
Descriptors	• Pain/ discomfort

Table 10-45 Summary of the Importance of Play and Suggested Descriptors per Age Group

Importance of Play (0-12 months)	• After the first month it becomes priority to explore, learn, and grow. Play is very important but only after the first month. • Important for children to play • Meaningful interaction with people and the environment through play (and therefore often movement) is essential for normal development, improving mood and bonding. Function or Activities of Daily Living (ADL) in children is really play. Independence in ADL is one of the features of good QOL in adults, so presumably is important in children too. Play is age-dependent, so this needs to be specified to cater for all developmental stages from 0-12 months. • Ability to play is an important sign of well-being. • Healthy play is a good feature of childhood.
Descriptors	• 0-6 months: able to follow objects, things/persons moving around then able to take/touch objects with hands/feet. 6-12 months: able to use objects to see what happens -throwing a ball, playing with food. • Able to play. • Able to engage in age-appropriate play (with examples for each age groups) • Playing with toys, and starting to interact with other infants and children. • Engaging in an enjoyable activity.
Importance of Play (12-24 months)	• Play is a necessary activity for growing - a healthy child plays. • Play is a child's function, their ADLs and therefore integral to QoL. Exploratory play in this age group is essential for sensory, cognitive and motor development. • Includes socialisation, communication and motor and cognitive skills. • Ability to play is an important indicator of good health. • Play suggests good interaction and is a normal activity for children. • Healthy, happy children with good HRQoL would spend most of their day engaged in play.
Descriptors	• Will to play (explore) with anything. • Able to engage in play behaviours (not necessarily through limb movement). • Able to play alongside other children, engages in one on one activity with caregiver. • Playing with other children, playing with toys and any objects in environment. • Engaging in a specific activity for enjoyment.
Importance of UA (12-24 months)	• Ability to engage in UA is an indicator of good health and overlaps with play.
Descriptors	• Play

Importance of Play (24-36 months)	• Play is function in a child, and ability to function relates to QoL. • Normal play is the work of childhood, and QoL should enable playing. • Child is essentially learning through play.
Descriptors	• Able to play physically/cognitively at an age/condition appropriate level. • Imaginative play by himself and with others, takes turns. • Playing normally with other children and with the toys. • Using physical abilities, problem solving skills and language to engage joyfully with other children.
Importance of UA (24-36 months)	• This relates to ADL and developing independence, which impacts on QOL. • Able to perform certain gross motor and fine motor activities. • As a general indicator of good health.
Descriptors	• Walk up and down stairs without help, jump with 2 feet, throw a ball, stack 6 blocks, draw a vertical line. • Pertaining to some independence.

Table 10-46 Summary of the Importance of Relationships and Suggested Descriptors per Age Group

Importance of Relationships (0-12 months)	• Bonding/communication between the child and family (particularly the mother) is integral to QOL. The child cannot be meaningfully separated from the parent at this young stage, and is dependent on them for all their care. A good relationship/bond will therefore likely equate to better care, more responsive handling, optimised development, and better QOL. • Early relationships are indicative of emotional wellbeing. • Ability to attach to caregivers appropriately reflects health of child/ parent dyad- I don't think this can be separated. • The quality of relationships with family and other children is an important aspect of QoL. • Important for growth, development and future relationships.
Descriptors	• Recognises and responds positively to mother/significant carer. • Able to interact and form relationships with significant others. • Making eye contact well, responding appropriately to speech, recognising individuals and family members and enjoying social contact.
Importance of Relationships (12-24 months)	• This includes items related to communication and socialising with peers, parents, siblings, family etc. The young child is still dependent on their carer (often the mother), and appropriate strong parental bonds are directly related to a child's sense of security and well-being. • Ability to interact appropriately with others is important for emotional, social and cognitive well-being. • Ability to bond with others is an important indicator of good health. • Humans need good relationships to be happy most of the time. • Need them to develop and live within the family structure.
Descriptors	• Able to communicate basic needs to carers. Able to play/socialise with other children of similar ages. Displays a strong bond with carer. • Recognises and responds with affection to family and close friends. • Recognises people, interacts well with family and close friends. • Knows family and recognises a stranger
Importance of Socializing (12-24 months)	• One of the life tasks of this age-group is socializing with other people and is one of the biggest learning challenges. • Child starting to learn how to behave in the company of others.
Descriptors	• Developing a sense of self in relation to other people. • Acting appropriately with other people.
Importance of Relationships (24-36 months)	• Early relationships indicative of emotional well-being. • People relate to each other and QoL is related to quality of relationships.

Descriptors	• Strong bonds with family and close friends. • Relating well to family, friends and peers and communicating well.
Importance of Socializing (24-36 months)	• Communicating with peers/carers and developing social play is important. • As a general indicator of good health • Learning acceptable behaviour towards others.
Descriptors	• Able to communicate at an age- and condition appropriate level with other children and carer/s. • Ability to play and interact with others. • Able to engage with other children.

Table 10-47 Summary of the Importance of Sickness and Suggested Descriptors per Age Group

Importance of Sickness (0-12 months)	• There are different types of sickness: flu or tumour for instance. The sickness is to be identified and managed. • Sickness has the potential to impact negatively on the baby. • Parents impression of child being “sick" is subjective but useful. • Sickness would indicate a decrease in HRQoL.
Descriptors	• 0-6 months: sickness identified according to complaints of the mother. 6-12 months: sickness identified according to complaints of the child. • Having health impairments. • Generally healthy apart from occasional minor illnesses. • Unwell with temperature or vomiting or continuous crying or diarrhoea or lethargy. • Can compromise development.
Importance of Sickness (12-24 months)	• Any sickness has to be considered at any age. • Has the potential to impact negatively on the baby.
Descriptors	• Having a mild (e.g. Flu) or severe (e.g., gastroenteritis, allergy, cancer) sickness. • Generally well apart from occasional minor childhood illnesses.
Importance of Sickness (24-36 months)	• As a general indicator of poor health.
Descriptors	• Generally healthy apart from occasional minor illnesses

Table 10-48 Summary of the Importance of Sleeping and Suggested Descriptors per Age Group

Importance of Sleeping (0-12 months)	• A baby who does not sleep does not grow or develop appropriately and is often miserable. Also, a crying, not sleeping baby leads to a sleep-deprived mother, with resulting problems of attachment which could then negatively impact on the mother-infant bond and thus on HRQoL. • Sleeping like feeding is vitally important for the young child and its caregivers • Infants need a lot of sleep for optimum health and development. Sleep disruption indicate poor physical or emotional health. • The quality of the child's sleep affects not only the child, but also those around them. • A healthy and content baby would have a good sleep pattern. • Essential for life.
Descriptors	• This would be age-dependent, could categorise into number of hours continuous sleep per night/number of awakenings? Or good QOL might require - falls asleep easily and generally sleeps well. • Has a regular sleep pattern that is age appropriate. • Regular uninterrupted sleep without disturbances and nightmares. • Eyes closed body still for an hour or more.
Importance of Sleeping (12-24 months)	• A child who does not sleep is often miserable, people in the household also cannot sleep properly and relationships become dysfunctional, leading to poor QOL amongst all parties. • Good quality of sleep is good for the child and the family, and again suggests an absence of discomfort.
Descriptors	• Able to fall asleep easily and stay asleep for most of the night. • Has regular sleep times during the day, sleeps well at night. • Sleeps well without disturbance; normal sleep patterns; no abnormal waking or bad nightmares. • Sleeps through the night
Importance of Sleeping (24-36 months)	• Good sleep is a feature of health and quality of life for the child and his / her family.
Descriptors	• Good sleep patterns without regular waking at night. • Enough for age to maintain healthy body and mind.

HRQoL-10D-IT

(Infant & Toddler) – Alpha Draft

Health Questionnaire

Experimental Version

Script for proxy version of the HRQoL-10D-IT

For children aged 0-36 months

(The purpose of this questionnaire is to explore how a care-giver or someone who knows the child well (proxy), would rate the health status of the child. The proxy should not answer on behalf of the child, but rather rate the child's health status as the proxy sees it)

HRQoL-10D-IT

Describing the child's health today

Under each heading, mark the ONE box that best describes how **you** would describe the health state of the child TODAY.

Movement

(0-1 month: grasping, sucking) (2-5 months: plays while on tummy)

(6-7 months: sitting)(9-11 months: crawling and standing) (12-36 months: walking)

He/she has no problems with movement ❑

He/she has some problems with movement ❑

He/she has a lot of problems with movement ❑

Helping with daily activities

(Age appropriate assistance with washing, dressing and toileting)

He/she has no problems helping with daily activities ❑

He/she has some problems helping with daily activities ❑

He/she has a lot of problems helping with daily activities ❑

Play (Enjoys playing with objects or toys)

He/she has no problems playing ❑

He/she has some problems playing ❑

He/she has a lot of problems playing ❑

Pain (painful behaviour includes: grimace, restless movement, inconsolable cry)

He/she has no pain ❑

He/she has some pain ❑

He/she has a lot of pain ❑

Controlling Emotions (settles easily with familiar people, touch or sound)

He/she has no problems controlling his/her emotions ❑

He/she has some problems controlling his/her emotions ❑

He/she has a lot of problems controlling his/her emotions ❑

Relationships *(Interacts with family members is an age-appropriate manner)*

He/she has no problems with relationships ❑

He/she has some problems with relationships ❑

He/she has a lot of problems with relationships ❑

Behaviour *(Aware of different situations and able to respond appropriately to new places and people)*

He/she has no problems with behaviour ❑

He/she has some problems with behaviour ❑

He/she has a lot of problems with behaviour ❑

Communication

(0-6 months: cooing, squealing, eye contact, smiling) (7-12 months: 'gaga' uses gestures like pointing) (12-19 months: single words) (19-24 months: puts two words together)(25-36 months: starts telling stories)

He/she has no problems with communication ❑

He/she has some problems with communication ❑

He/she has a lot of problems with communication ❑

Eating (adequate oral intake to sustain growth)

He/she has no problems with eating ❑

He/she has some problems with eating ❑

He/she has a lot of problems with eating ❑

Sleeping (*falls asleep easily, has restful uninterrupted sleep and enough sleep*)

(0-3 months: 16-20 hours a day) (3-6 months 15-16 hours a day) (6-12 months: 11-14 hours a day) (12-36 months: 10-13 hours a day)

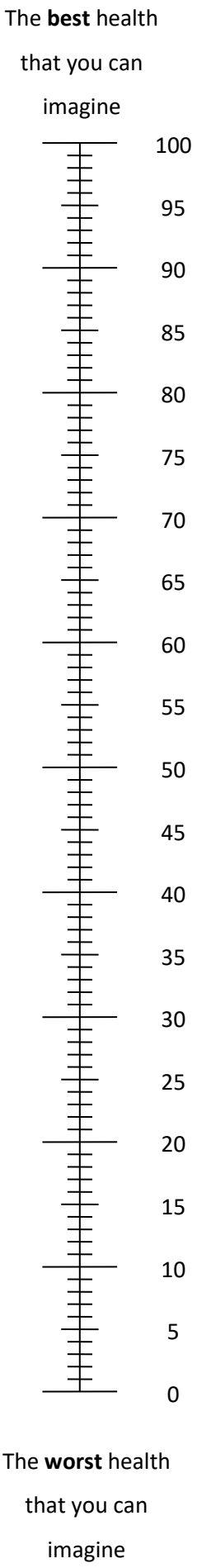
He/she has no problems with sleeping ❑

He/she has some problems with sleeping ❑

He/she has a lot of problems with sleeping ❑

How good is the health of the child TODAY

- We would like to know how good or bad you think the child's health is TODAY.
- This line is numbered 0 to 100.
- 100 means the <u>best</u> health you can imagine.
  0 means the <u>worst</u> health you can imagine.
- Please, mark an X on the line that shows how good or bad you think the child's health is TODAY.



10.14 Appendix 14 Institutional Approval

Western Cape Government
Health

Dr AS Booysen
Manager: Medical Services
Email: Tony.Booysen@Westerncape.gov.za
Tel: +27 21 658 5788 fax: +27 21 658 5166
RXH: RCC36

Ms J Verstraete
Red Cross War Memorial Children's Hospital

Dear Ms J Verstraete

APPROVAL OF RESEARCH

PROJECT TITLE: DEVELOPMENT OF AN ENGLISH HEALTH-RELATED QUALITY OF LIFE (HRQOL) INSTRUMENT FOR CHILDREN UNDER SEVEN YEARS OF AGE, DERIVED FROM THE EQ-5D-Y, TO BE COMPLETED BY PROXY

It is a pleasure to inform you that approval is hereby granted to conduct the above-mentioned study at Red Cross War Memorial Children's Hospital.

Yours sincerely,

Dr AS Booysen
Manager: Medical Services
Date: 24.08.16

10.15 Appendix 15 Informed Consent for Testing of Alpha Draft

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences

School of Health and Rehabilitation Sciences

Division of Physiotherapy
F45 Old Main Building, Groote Schuur Hospital,
Observatory 7925
Tel: +27 (0) 21 406 62505
Fax: +27 (0) 21 406 6323

Informed consent from caregivers taking part in the study

Information Sheet

Title of the Study: Testing a preliminary version of a Health-Related Quality of Life measure for very young children.

Dear Parents,

I am doing a research project as part of my PhD in physiotherapy. I have developed a new measure of Health-Related Quality of Life for children between 0-36 months. I want to test which questions need to stay in the final measure.

I will ask you to fill-in a few questions about your child's quality of life. There are ten questions about how your child moves, helps with daily activities, playing, pain, emotional regulation, relationships, behaviour, communication, eating and sleep. This should not take longer than 10 minutes. The other caregivers of children under three are being invited to take part at this facility.

It is your choice to take part in this study and you do not have to agree if you don't want to. If you choose not to take part in the study, nothing bad will happen to you or your child. If you agree now but decide later that you don't want to do it anymore, you can let us know and all of the information that you have given us will be taken out of the study. We will be grateful if you would help us by agreeing to let us interview you. If you decide to be part of the study, the treatment and care that your child is getting will not be changed in any way and will carry on as normal.

Your child's name will be written on the form. If we find anything that worries us we can let you know. We will talk to you about the problem and if you agree we can ask a doctor or a therapist to assess your child. All the information that you give will be confidential. Your child's name will be deleted when we study the information. If we publish what we find, nobody will know that you took part or what you answered. The information will be collected by myself and stored onto a secure computer with a password. The information that you give will only be used for this study.

There are no risks in taking part in this study. You will not be given any money for being part of the study. I will be comparing the information that you give me to caregivers of other children who are sick. I hope that this will help us to understand the quality of life of children better and to improve the way we look after all children in the future.

If you have any questions or concerns about the study you may contact the researcher or the supervisor:

Researcher

Janine Verstraete

Red Cross War Memorial Children's Hospital

Division of Physiotherapy

S13 Out Patients Building

Klipfontein Road

Rondebosch

Tel: 021 658 5033

Cell: 082 840 9293

Supervisor

Professor J. Jelsma

University of Cape Town

Department of Health &Rehabilitation Sciences

Division of physiotherapy

F45 Old Main Building

Groote Schuur Hospital

Observatory

Tel: 021-406 6401

If you have any questions about your rights or welfare as a research participant please contact:

Professor M. Blockman

The University of Cape Town

Faculty of Health Sciences Human Research Ethics Committee

Tel: 021 406 6492

Room: E52.24 Old Main Building

Consent Form

Please can you read through the table below and mark off your answer with an X

Declaration	Yes	No
I have read through the information provided and understand it.		
I understand that my consent is required.		
I understand that it is my choice to take part and I can refuse my consent without any consequences to myself or my child.		
I understand that not agreeing to take part in the study will not change the way they are treating my child now or in the future.		
I understand that nobody will know that either my child or I took part in the study if it is published.		
I consent to taking part in this research of my own free will.		

Signed:

_____ _____

Caregivers signature Date

_____ _____

Researcher signature Date

HRQoL-6D-IT

(Infant & Toddler) – Beta Draft

Health Questionnaire

Experimental Version

Script for proxy version of the HRQoL-6D-IT

For children aged 0-36 months

(The purpose of this questionnaire is to explore how a care-giver or someone who knows the child well (proxy), would rate the health status of the child. The proxy should not answer on behalf of the child, but rather rate the child's health status as the proxy sees it)

HRQoL-6D-IT

Describing the child's health today

Under each heading, mark the ONE box that best describes how **you** would describe the health state of the child TODAY.

Movement *(Moves about at an age appropriate level)*

He/she has no problems with movement ❑

He/she has some problems with movement ❑

He/she has a lot of problems with movement ❑

Play *(Enjoys playing with objects or toys at an age appropriate level)*

He/she has no problems playing ❑

He/she has some problems playing ❑

He/she has a lot of problems playing ❑

Pain *(Painful behaviour includes: grimace, restless movement, inconsolable cry)*

He/she has no pain ❑

He/she has some pain ❑

He/she has a lot of pain ❑

Relationships *(Interacts with family members in an age-appropriate manner)*

He/she has no problems with relationships ❑

He/she has some problems with relationships ❑

He/she has a lot of problems with relationships ❑

Communication *(Communicates at an age appropriate level)*

He/she has no problems with communication ❑

He/she has some problems with communication ❑

He/she has a lot of problems with communication ❑

Eating *(Adequate oral intake to sustain growth at an age appropriate level)*

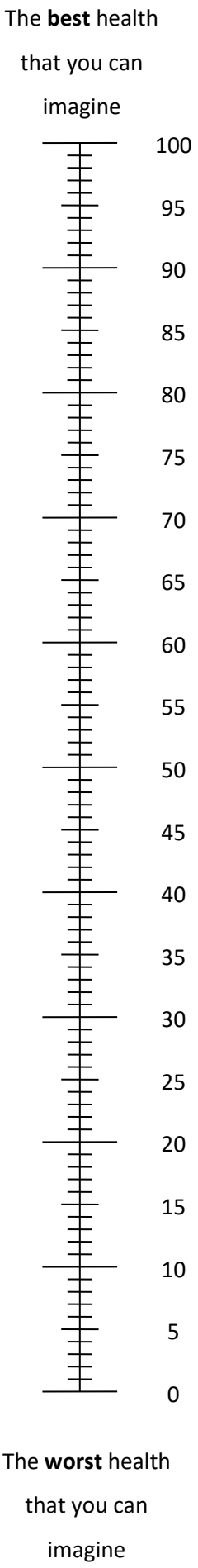
He/she has no problems with eating ❑

He/she has some problems with eating ❑

He/she has a lot of problems with eating ❑

How good is the health of the child TODAY

- We would like to know how good or bad you think the child's health is TODAY.
- This line is numbered 0 to 100.
- 100 means the <u>best</u> health you can imagine.
  0 means the <u>worst</u> health you can imagine.
- Please, mark an X on the line that shows how good or bad you think the child's health is TODAY.



10.17 Appendix 17 Informed Consent for Beta Draft Testing

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences

School of Health and Rehabilitation Sciences

Division of Physiotherapy
F45 Old Main Building, Groote Schuur Hospital,
Observatory 7925
Tel: +27 (0) 21 406 62505
Fax: +27 (0) 21 406 6323

Informed consent from caregivers taking part in the study

Information Sheet

Title of the Study: Testing a preliminary version of a Health-Related Quality of Life measure for very young children.

Dear Parents,

I am doing a research project as part of my PhD in physiotherapy. I have developed a new measure of Health-Related Quality of Life for children between 0-36 months. I want to test which questions need to stay in the final measure.

I will ask you to fill-in a few questions about your child's quality of life. There are six questions about: how your child moves, plays, pain, relationships, communication and eating. This should not take longer than 10 minutes. The other caregivers of children under three are being invited to take part at this facility.

It is your choice to take part in this study and you do not have to agree if you don't want to. If you choose not to take part in the study, nothing bad will happen to you or your child. If you agree now but decide later that you don't want to do it anymore, you can let us know and all of the information that you have given us will be taken out of the study. We will be grateful if you would help us by agreeing to let us interview you. If you decide to be part of the study, the treatment and care that your child is getting will not be changed in any way and will carry on as normal.

Your child's name will be written on the form. If we find anything that worries us we can let you know. We will talk to you about the problem and if you agree we can ask a doctor or a therapist to assess your child. All the information that you give will be confidential. Your child's name will be deleted when we study the information. If we publish what we find, nobody will know that you took part or what you answered. The information will be collected by myself and stored onto a secure computer with a password. The information that you give will only be used for this study.

There are no risks in taking part in this study. You will not be given any money for being part of the study. I will be comparing the information that you give me to caregivers of other children who are sick. I hope that this will help us to understand the quality of life of children better and to improve the way we look after all children in the future.

If you have any questions or concerns about the study you may contact the researcher or the supervisor:

Researcher	Supervisor
Janine Verstraete	Professor J. Jelsma
Red Cross War Memorial Children's Hospital	University of Cape Town
Division of Physiotherapy	Department of Health &Rehabilitation Sciences
S13 Out Patients Building	Division of physiotherapy
Klipfontein Road	F45 Old Main Building
Rondebosch	Groote Schuur Hospital
Tel: 021 658 5033	Observatory
Cell: 082 840 9293	Tel: 021-406 6401

If you have any questions about your rights or welfare as a research participant please contact:

Professor M. Blockman

The University of Cape Town

Faculty of Health Sciences Human Research Ethics Committee

Tel: 021 406 6492

Room: E52.24 Old Main Building

Consent Form

Please can you read through the table below and mark off your answer with an X

Declaration	Yes	No
I have read through the information provided and understand it.		
I understand that my consent is required.		
I understand that it is my choice to take part and I can refuse my consent without any consequences to myself or my child.		
I understand that not agreeing to take part in the study will not change the way they are treating my child now or in the future.		
I understand that nobody will know that either my child or I took part in the study if it is published.		
I consent to taking part in this research of my own free will.		

Signed:

_____ _____

Caregivers signature Date

_____ _____

Researcher signature Date

10.18 Appendix 18 Informed Consent for Validity and Reliability Testing

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences

School of Health and Rehabilitation Sciences

Division of Physiotherapy
F45 Old Main Building, Groote Schuur Hospital,
Observatory 7925
Tel: +27 (0) 21 406 62505
Fax: +27 (0) 21 406 6323

Informed consent from caregivers taking part in the study

Information Sheet

Title of the Study: Development of an English Health-Related Quality of Life instrument for children under three years of age, derived from the EQ-5D-Y, to be completed by proxy.

Dear Parent,
I am doing a research project as part of my PhD in physiotherapy. I want to look at how you answer questions about your child's Health-Related Quality of Life. I am asking you to take part in this research by answering five short questionnaires about your child.
I want to know how the answers from the questionnaires compare to each other. I will ask you to fill-in a short form about how your child moves, plays, if they have pain, their relationships and how they are eating. This should not take longer than 5 minutes. If your child is at a day-care centre you will fill-in this same questionnaire again in a week. You will then need to fill in a similar questionnaire about your health with relation to how you move, self-care, daily activities, anxiety/depression and pain. The third questionnaires should take 15 minutes to complete and asks about how your child does things for their age. There is a scale asking you to rate your child's pain on a scale and a short form about what your child has had to eat or drink. I will also collect other general information about you and your child. The whole process should take no longer than 30 minutes. All the other caregivers of children under three are being invited to take part at this facility and others.
It is your choice to take part in this study and you do not have to agree if you don't want to. If you do not agree, nothing bad will happen to you or your child. If you agree now but decide later that you don't want to do it anymore. You can let us know and all of the information that you have given us will be taken out of the study. We will be thankful if you would help us by agreeing to let us interview you. If you agree to help us, the treatment that your child is getting will not be changed and will carry on as normal.
Your child's name will be written on the form. If we find anything that worries us we can let you know. We will talk to you about the problem and if you agree we can ask a doctor or a therapist to assess your child.
All the information that you give will be confidential. Your child's name will be deleted when we study the information. If we publish what we find, nobody will know that you took part or what you answered. The information will be collected by myself and stored onto a secure computer with a password. The information that you give will only be used for this study.
There are no risks in taking part in this study. You will not be given any money for being part of the study. I will be comparing the information that you give me to caregivers of other children who are acutely sick and in hospital, chronically ill or attending a day-care centre. I hope that this will help us to understand the quality of life of children better and to improve the way we look after all children in the future.
If you have any questions or concerns about the study you may contact the researcher or the supervisor:

Researcher
Janine Verstraete
Red Cross War Memorial Children's Hospital
Division of Physiotherapy
S13 Out Patients Building
Klipfontein Road
Rondebosch
Tel: 021 658 5033
Cell: 082 840 9293

Supervisor
Professor J. Jelsma
University of Cape Town
Department of Health &Rehabilitation Sciences
Division of physiotherapy
F45 Old Main Building
Groote Schuur Hospital
Observatory
Tel: 021-406 6401

If you have any queries about your rights or welfare as a research participant please contact;
Professor M. Blockman
The University of Cape Town
Faculty of Health Sciences Human Research Ethics Committee
Tel: 021 406 6492
Room: E52.24 Old Main Building

Consent Form
Please can you read through the table below and mark off your answer with an X

Declaration	Yes	No
I have read through the information provided and understand it.		
I understand that my consent is required.		
I understand that it is voluntary to participate and I can refuse my consent without any consequences to myself or my child.		
I understand that refusing to give consent will not affect the current or future health care of my child.		
I understand that neither my child nor I will be identified should this research study be published.		
I consent to taking part in this research of my own free will.		

Signed:

Caregivers signature _____ Date _____

Child's Name _____

Researcher signature _____

10.19 Appendix 19 General Information

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences

School of Health and Rehabilitation Sciences
Division of Physiotherapy

Division of Physiotherapy
F45 Old Main Building, Groote Schuur Hospital,
Observatory 7925
Tel: +27 (0) 21 406 62505
Fax: +27 (0) 21 406 6323

General Information for Caregiver and Child

Child's Name _____ Today's Date _____

Child's Date of Birth: _____

Please Circle the correct response, where appropriate:

Was your child born more than 3 weeks Premature? Yes No

If Yes, please state how many weeks: _____

Institution: Acute Care Chronic Care Day Care Centre/Play group

Relationship of Caregiver to Child: Mother Father Aunt
Uncle Grandmother Grandfather
Other: _____

Which suburb do you live in? _

Please, list if your child has any medical condition(s) diagnosed by a doctor: _____

_____

Please, list any medication that your child has received today: _____

_

_

Is there anything that has happened in the last week that upset your child? e.g. starting a new school, separation from a loved one etc.

YES/NO Please specify: _____

Is there anything that has happened in the last week that has upset you? e.g. Starting a new job, loss of a loved one etc.

YES/NO Please specify: _____

Please, list if you have any medical condition(s) diagnosed by a doctor::_____

_

10.20 Appendix 20 Delta Draft of the HRQoL-6D-IT

HRQoL-6D-IT

(Infant & Toddler) – Delta Draft

Health Questionnaire

Experimental Version

Script for proxy version of the HRQoL-6D-IT

For children aged 1-36 months

(The purpose of this questionnaire is to explore how a care-giver or someone who knows the child well (proxy), would rate the health status of the child. The proxy should not answer on behalf of the child, but rather rate the child's health status as the proxy sees it)

HRQoL-6D-IT

Describing the child's health today

Under each heading, mark the ONE box that best describes how **you** would describe the health state of the child TODAY.

Movement *(Moves about at an age appropriate level)*

He/she has no problems with movement ❑

He/she has some problems with movement ❑

He/she has a lot of problems with movement ❑

Play *(Enjoys playing with objects or toys at an age appropriate level)*

He/she has no problems playing ❑

He/she has some problems playing ❑

He/she has a lot of problems playing ❑

Pain *(Painful behaviour includes: grimace, restless movement, inconsolable cry)*

He/she has no pain ❑

He/she has some pain ❑

He/she has a lot of pain ❑

Relationships *(Interacts with family members in an age-appropriate manner)*

He/she has no problems with relationships ❑

He/she has some problems with relationships ❑

He/she has a lot of problems with relationships ❑

Communication *(Communicates at an age appropriate level)*

He/she has no problems with communication ❑

He/she has some problems with communication ❑

He/she has a lot of problems with communication ❑

Eating *(Adequate oral intake to sustain growth at an age appropriate level)*

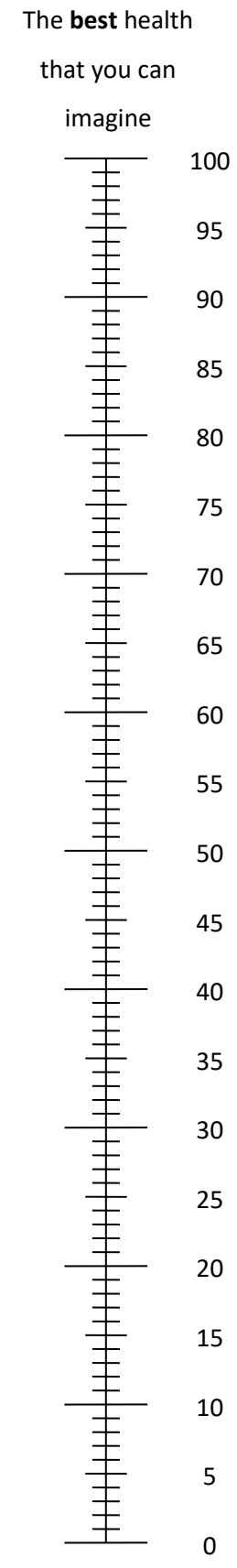
He/she has no problems with eating ❑

He/she has some problems with eating ❑

He/she has a lot of problems with eating ❑

How good is the health of the child TODAY

- We would like to know how good or bad you think the child's health is TODAY.
- This line is numbered 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Please, mark an X on the line that shows how good or bad you think the child's health is TODAY.



10.21 Appendix 21 Example of Ages and Stages Questionnaire

ASQ-3

16 Month Questionnaire

15 months 0 days

through 16 months 30 days

On the following pages are questions about activities children may do. Your child may have already done some of the activities described here, and there may be some your child has not begun doing yet. For each item, please fill in the circle that indicates whether your child is doing the activity regularly, sometimes, or not yet.

Child's name: _____

Thank you for your participation!

COMMUNICATION

	YES	SOMETIMES	NOT YET	
1. Does your child point to, pat, or try to pick up pictures in a book?	◯	◯	◯	___
2. Does your child say four or more words in addition to "Mama" and "Dada"?	◯	◯	◯	___
3. When your child wants something, does she tell you by *pointing* to it?	◯	◯	◯	___
4. When you ask your child to, does he go into another room to find a familiar toy or object? *(You might ask, "Where is your ball?" or say, "Bring me your coat," or "Go get your blanket.")*	◯	◯	◯	___
5. Does your child imitate a two-word sentence? For example, when you say a two-word phrase, such as "Mama eat," "Daddy play," "Go home," or "What's this?" does your child say both words back to you? *(Mark "yes" even if her words are difficult to understand.)*	◯	◯	◯	___
6. Does your child say eight or more words in addition to "Mama" and "Dada"?	◯	◯	◯	___
		COMMUNICATION TOTAL		___

GROSS MOTOR

	YES	SOMETIMES	NOT YET	
1. Does your child stand up in the middle of the floor by himself and take several steps forward?	◯	◯	◯	___
2. Does your child climb onto furniture or other large objects, such as large climbing blocks?	◯	◯	◯	___
3. Does your child bend over or squat to pick up an object from the floor and then stand up again without any support?	◯	◯	◯	

GROSS MOTOR *(continued)*

	YES	SOMETIMES	NOT YET	
4. Does your child move around by walking, rather than crawling on her hands and knees?	○	○	○	___
5. Does your child walk well and seldom fall?	○	○	○	___
6. Does your child climb on an object such as a chair to reach something he wants (for example, to get a toy on a counter or to "help" you in the kitchen)?	○	○	○	___
		GROSS MOTOR TOTAL		___

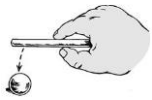
FINE MOTOR

	YES	SOMETIMES	NOT YET	
1. Does your child help turn the pages of a book? *(You may lift a page for her to grasp.)*	○	○	○	___
2. Does your child throw a small ball with a forward arm motion? *(If he simply drops the ball, mark "not yet" for this item.)* 	○	○	○	___
3. Does your child stack a small block or toy on top of another one? *(You could also use spools of thread, small boxes, or toys that are about 1 inch in size.)*	○	○	○	___
4. Does your child stack three small blocks or toys on top of each other by herself?	○	○	○	___
5. Does your child make a mark on the paper with the *tip* of a crayon (or pencil or pen) when trying to draw? 	○	○	○	___
6. Does your child turn the pages of a book by himself? *(He may turn more than one page at a time.)*	○	○	○	___
		FINE MOTOR TOTAL		___

PROBLEM SOLVING

	YES	SOMETIMES	NOT YET	
1. After you scribble back and forth on paper with a crayon (or pencil or pen), does your child copy you by scribbling? *(If she already scribbles on her own, mark "yes" for this item.)*	○	○	○	___
2. Can your child drop a crumb or Cheerio into a small, clear bottle (such as a plastic soda-pop bottle or baby bottle)?	○	○	○	___
3. Does your child drop several small toys, one after another, into a container like a bowl or box? *(You may show him how to do it.)*	○	○	○	___

PROBLEM SOLVING *(continued)*

	YES	SOMETIMES	NOT YET	
4. After you have shown your child how, does she try to get a small toy that is slightly out of reach by using a spoon, stick, or similar tool? 	○	○	○	___
5. Without your showing him how, does your child scribble back and forth when you give him a crayon (or pencil or pen)?	○	○	○	___ *
6. After a crumb or Cheerio is dropped into a small, clear bottle, does your child turn the bottle upside down to dump it out? *(You may show her how.)*	○	○	○	___

PROBLEM SOLVING TOTAL ___

**If Problem Solving Item 5 is marked "yes," mark Problem Solving Item 1 as "yes."*

PERSONAL-SOCIAL

	YES	SOMETIMES	NOT YET	
1. Does your child feed himself with a spoon, even though he may spill some food?	○	○	○	___
2. Does your child help undress herself by taking off clothes like socks, hat, shoes, or mittens?	○	○	○	___
3. Does your child play with a doll or stuffed animal by hugging it?	○	○	○	___
4. While looking at himself in the mirror, does your child offer a toy to his own image?	○	○	○	___
5. Does your child get your attention or try to show you something by pulling on your hand or clothes?	○	○	○	___
6. Does your child come to you when she needs help, such as with winding up a toy or unscrewing a lid from a jar?	○	○	○	___

PERSONAL-SOCIAL TOTAL

10.22 Appendix 22 Ages and Stages Questionnaire Report Form for Caregivers of Typically Developing Children

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
School of Health and Rehabilitation Sciences
Division of Physiotherapy

Division of Physiotherapy
F45 Old Main Building, Groote Schuur Hospital,
Observatory 7925
Tel: +27 (0) 21 406 62505
Fax: +27 (0) 21 406 6323

Dear

Report of Results from the Ages and Stages Questionnaire

The results reported on are in response to the answers which you provided on the Ages and Stages Questionnaire. This questionnaire about children's development has been used for more than 20 years to make sure children are developing well. As it is a screening tool it only provides a quick look at how your child is doing in important areas, such as communication, physical ability, social skills, and problem-solving skills. It can further help identify your child's strengths as well as any areas where your child may need support.

Your child's development for each area is summarised below.
I have attached a guide of activities which you can enjoy together with your child in order to help them continue to thrive with both their learning and development.

	Your Child's Performance
Communication	_____
Gross Motor Skills	_____
Fine Motor Skills	_____
Social Skills	_____
Problem Solving Skills	_____

I would like to thank you for your participation in my study, and helping me to realise my dream of completing my PhD.
Please do not hesitate to contact me if you have any queries or concerns.

Kind Regards

Janine Verstraete
victor_janine@yahoo.com
082 840 9293

10.23 Appendix 23 Example of Ages and Stages Questionnaire Activity Sheet

Activities for Infants 12-16 Months Old

ASQ-3™

Babies love games at this age (Pat-a-Cake, This Little Piggy). Try different ways of playing the games and see if your baby will try it with you. Hide behind furniture or doors for Peekaboo; clap blocks or pan lids for Pat-a-cake.	Make puppets out of a sock or paper bag—one for you and one for your baby. Have your puppet talk to your baby or your baby's puppet. Encourage your baby to "talk" back.	To encourage your baby's first steps, hold your baby in standing position, facing another person. Have your baby step toward the other person to get a favorite toy or treat.	Give your baby containers with lids or different compartments filled with blocks or other small toys. Let your baby open and dump. Play "putting things back." This will help your baby learn how to release objects where he wants them.	Loosely wrap a small toy in a paper towel or facial tissue without tape. Your baby can unwrap it and find a surprise. Use tissue paper or wrapping paper, too. It's brightly colored and noisy.
Babies enjoy push and pull toys. Make your own pull toy by threading yogurt cartons, spools, or small boxes on a piece of yarn or soft string (about 2 feet long). Tie a bead or plastic stacking ring on one end for a handle.	Tape a large piece of drawing paper to a table. Show your baby how to scribble with large nontoxic crayons. Take turns making marks on the paper. It's also fun to paint with water.	Arrange furniture so that your baby can work her way around a room by stepping across gaps between furniture. This encourages balance in walking.	Babies continue to love making noise. Make sound shakers by stringing canning rims together or filling medicine bottles (with child-proof caps) with different-sounding objects like marbles, rice, salt, bolts, and so forth. Be careful to secure lids tightly.	This is the time your baby learns that adults can be useful! When your baby "asks" for something by vocalizing or pointing, respond to his signal. Name the object your baby wants and encourage him to communicate again—taking turns with each other in a "conversation."
Play the naming game. Name body parts, common objects, and people. This lets your baby know that everything has a name and helps her begin to learn these names.	Make an obstacle course with boxes or furniture so that your baby can climb in, on, over, under, and through. A big box can be a great place to sit and play.	Let your baby help you clean up. Play "feed the wastebasket" or "give it to Mommy or Daddy."	Make a surprise bag for your baby to find in the morning. Fill a paper or cloth bag with a soft toy, something to make a sound, a little plastic jar with a screw-top lid, or a book with cardboard pages.	Play "pretend" with a stuffed animal or doll. Show and tell your baby what the doll is doing (walking, going to bed, eating, dancing across a table). See if your baby will make the doll move and do things as you request. Take turns.
Cut up safe finger foods (do not use foods that pose a danger of your baby's choking) in small pieces and allow your baby to feed himself. It is good practice to pick up small things and feel different textures (bananas, soft crackers, berries).	Let your baby "help" during daily routines. Encourage your baby to "get" the cup and spoon for mealtime, to "find" shoes and coat for dressing, and to "bring" the pants or diaper for changing. Following directions is an important skill for your baby to learn.	Your baby is learning that different toys do different things. Give your baby a lot of things to roll, push, pull, hug, shake, poke, turn, stack, spin, and stir.	Most babies enjoy music. Clap and dance to the music. Encourage your baby to practice balance by moving forward, around, and back. Hold her hands for support, if needed.	Prepare your baby for a future activity or trip by talking about it beforehand. Your baby will feel like a part of what is going on rather than being just an observer. It may also help reduce some fear of being "left behind."

10.24 Appendix 24 FLACC Scale

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FLACC SCALE

Please circle the description which is applicable to your child for each heading.

Behavioural Observation Pain Rating Scale

	Score		
Categories	0	1	2
Face	No particular expression or smile; disinterested	Occasional grimace, frown, withdrawn	Frequent to constant frown, clenched jaw, quivering chin
Legs	No position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No crying (awake or asleep)	Moans or whimpers, occasional complaint	Crying, steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or talking to. Distractible	Difficult to console or comfort

10.25 Appendix 25 Neonatal Infant Pain Scale (NIPS)

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Neonatal Infant Pain Scale NIPS

Please circle the description which best describes your child for each category.

NPS	0 point	1 point	2 points
Facial expression	Relaxed	Contracted	
Cry	Absent	Mumbling	Vigorous
Breathing	Relaxed	Different than basal	
Arms	Relaxed	Flexed/stretched	
Legs	Relaxed	Flexed/stretched	
Alertness	Sleeping/Calm	Uncomfortable	

10.26 Appendix 26 Dietary Information

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Dietary Information

Please circle the correct response:

Is your child eating or drinking as much as usual today?	YES	NO
Is your child eating or drinking as much as other children of the same age today?	YES	NO
Is your child eating or drinking at regular meal or snack times today?	YES	NO
Is your child chewing/sucking and swallowing their food well today?	YES	NO
Is your child able to feed comfortably without getting tired today?	YES	NO
Is your child receiving nutrition through a drip or feeding tube today?	YES	NO
Is your child bringing up their food/milk today?	YES	NO
Is your child gagging when food/milk is put into their mouth today?	YES	NO

SCORING

Answers 1-5: If YES give 1 point; if NO give 0 points

Answer 6-8: If YES give 0 points; If NO give 1 point

A higher score indicates better ability to eat

10.27 Appendix 27 EQ-5D-3L

Health Questionnaire

English version for the UK

(validated for Ireland)

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ❑

I have some problems in walking about ❑

I am confined to bed ❑

Self-Care

I have no problems with self-care ❑

I have some problems washing or dressing myself ❑

I am unable to wash or dress myself ❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑

I have some problems with performing my usual activities ❑

I am unable to perform my usual activities ❑

Pain/Discomfort

I have no pain or discomfort ❑

I have moderate pain or discomfort ❑

I have extreme pain or discomfort ❑

Anxiety/Depression

I am not anxious or depressed ❑

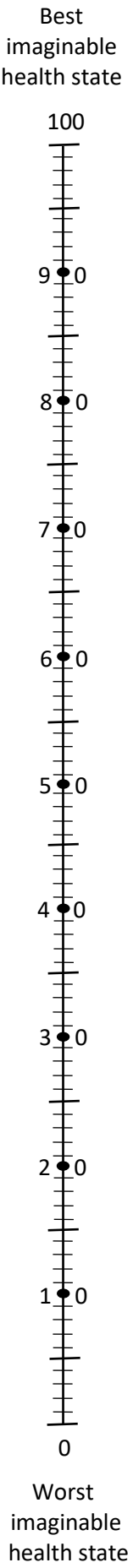
I am moderately anxious or depressed ❑

I am extremely anxious or depressed ❑

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



10.28 Appendix 28 Study Information for Caregivers

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Dear Parents

Participation in a research study measuring Health Related Quality of Life (HRQoL) in children under 3 years of age.

I am currently completing my PhD in Physiotherapy at the University of Cape Town. I have developed a new questionnaire to measure Health Related Quality of life in children under 3 years of age. This entails looking at how your child moves, plays, whether they have pain, their relationships and how they are eating. Because this is a new measure, we need to ask you more specific questions about your child's health and development to ensure that the new questionnaire is asking the correct questions.

Each of the children, under three years of age, at Noah's Ark will receive a research pack to be sent home inviting you to participate in the study. It is your choice to participate in the study and this will be explained to you in the informed consent. The research pack should take 20 – 30 minutes to complete. The pack will include some general questions about your child and his/her health. The HRQoL measure enquires about how the child is moving, playing, eating, communicating, pain and relationships. A developmental screening questionnaire (Ages and Stages) which asks you to complete questions about your child's gross and fine motor skills, communication, problem solving and personal-social skills. A pain scale and a questionnaire about your child's eating. There is also a HRQoL scale which enquires about your health (ability to walk, self-care, do usual activities, pain and anxiety or depression) as we are interested to see if there is any relationship between your health and your child's health. The research packs will be delivered to Noah's Ark on Tuesday the 14th March. I would like to ask all parents if they could please be returned to school by Thursday the 16th March. All parents who participate will receive a repeat measure of the HRQoL measure only, to complete one week later.

You will be asked to write your child's name on the pack as I will be giving you a summary of your child's development, as measured by the Ages and Stages Questionnaire, the following week. If there are any concerns noted about your child's development I will schedule a meeting with you to discuss the findings. Nobody else will know what your answers are and the name of your child will be deleted when captured for data analysis. Together with the report I will also send a list of recommended activities that you and your child can enjoy together.

I would like to take this opportunity to thank you the parents and Noah's Ark for your participation. Please do not hesitate to contact me if you require any further information regarding the study. My e-mail address is victor_janine@yahoo.com

Kind Regards

Mrs Janine Verstraete

10.29 Appendix 29 Information for the Repeat Measure of the HRQoL-6D-IT

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Title of the Study: Development of an English Health Related Quality of Life instrument for children under three years of age, derived from the EQ-5D-Y, to be completed by proxy.

Dear Parent,

Thank you, for the time you have taken to complete in the first round of data collection for my PhD study.

In the second round of the study you are invited to complete another copy of the Health Related Quality of Life measure for your child.

The purpose of this is to see whether the measure is able to give us reliable information.

We appreciate the time you have taken to complete this questionnaire.

If you have any questions or concerns about the study you may contact the researcher or the supervisor:

Researcher

Janine Verstraete

Red Cross War Memorial Children's Hospital

Division of Physiotherapy

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Klipfontein Road

Rondebosch

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